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THE USE OF SUTURE CONSTRICTION OF THE UPPER LOBE IN THE TREATMENT OF PULMONARY TUBERCULOSIS (PAULINO PROCEDURE)

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THE ideal type of thoracoplasty for advanced pulmonary tuberculosis, while retaining the relative safety of the multistaged selective thoracoplasty of the Alexander type,[1, 2] should if possible increase its effectiveness and should, in addition, be a single nondeforming operation with a minimal loss of the costal cage, and a maximal preservation of respiratory function. It should be applicable if necessary to bilateral disease.

In the summer of 1949, it was the privilege of one of us (P. T. D.) to observe in Rio de Janeiro the performance, by Dr. Fernando Paulino of that city, of a modified partial thoracoplasty and pneumonolysis which seemed to approach this ideal. This operation had been developed by Dr. Paulino and performed by him in approximately 20 cases. A review of his cases[4, 5] convinced us that the procedure merited further trial. The procedure employs the oldest, soundest, and most accurate method of constriction in surgery, namely, the suture ligature.

Since Sept. 16, 1949, we have employed the procedure thirty-four times, in thirty-one cases with gratifying results. Performed as a single operation with limited resection of the costal cage, deformity has been slight, and the loss of respiratory function has been minimal. This procedure has permitted bilateral operations in 3 cases. There have been few serious complications and, although it is too early to reach final conclusions, there is evidence that the control of the disease is as effective as, and possibly more effective than, that following the more extensive rib resection of the Alexander type.

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Collapse and compression of the diseased portions of the lung are obtained by a series of three No. 10 crochet cotton ligatures placed about the lung and the overlying parietal structures which have been freed from the chest wall according to the Carl Semb technique.[6] A limited rib resection is performed (1) to permit ready access for the pneumonolysis, (2) to obliterate the extrapleural space created by the pulmonary collapse, and (3) to prevent overexpansion of the lung below the level of the collapse.

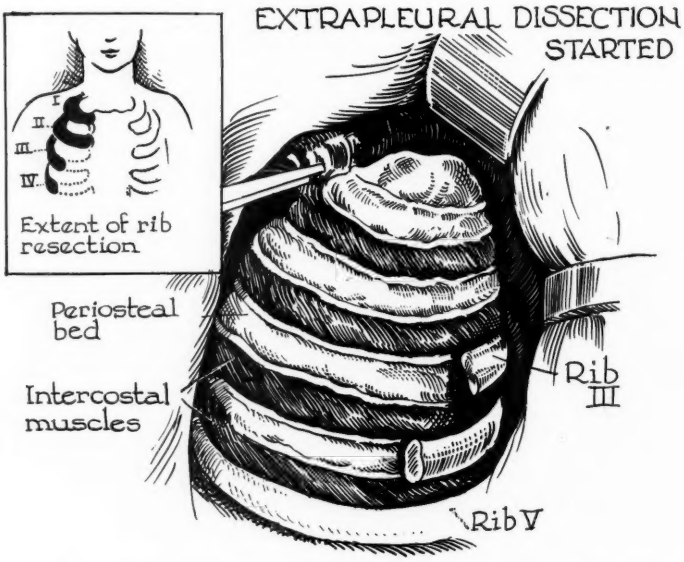

Fig. 1.—Technique of the Paulino procedure. Extent of the rib resection, and commencement of the extrafascial dissection, right lung.

TECHNIQUE

General anesthesia with intratracheal intubation is employed. We have placed the patient in the lateral decubitus position and employed a posterolateral parascapular incision. Dr. Paulino uses the face-down position.[4] Upon division of the muscles and retraction of the scapula, the rib cage is exposed. A subperiosteal resection of the first two ribs from the costal cartilages, the posterior two-thirds of the third rib, and the posterior half of the fourth rib is performed (Fig. 1). Posteriorly the ribs are removed only as far as the transverse processes of the vertebrae. The transverse processes are preserved. Beginning at the apex of the thorax an extrafascial pneumonolysis is performed by sharp and blunt dissection with division of the intercostal structures posteriorly and anteriorly (Fig. 1), according to the Semb technique.[6] The lung, overlying parietal pleura, and intercostal structures are freed to well below all gross lesions as determined by preoperative

roentgenography and operative palpation (Fig. 2). The dissection is limited inferiorly by the hilum of the lung, although it is possible to dissect somewhat below this point posteriorly if necessary to include lesions in the superior division of the lower lobe. If the collapse is carried to this point it may be wiser to remove a small posterior segment of the fifth rib.

The unique feature of the procedure is the method of achieving collapse, and preventing re-expansion, of the diseased lung. The apex of the pleura and the underlying lung is grasped with a large curved Kelly clamp. Beginning near the apex and concluding below the level of the grossly diseased lung, three concentric purse-string ligatures of No. 10 crochet cotton are placed about the lung and the overlying structures. Each ligature is caught in the pleura, the overlying tissues, or the lung itself at three or four points to prevent slipping. As each ligature is placed, it is drawn up snugly about the underlying diseased lung and tied (Fig. 3). Silver clips are placed on the lowest ligature as markers. At the conclusion of this stage of the operation all

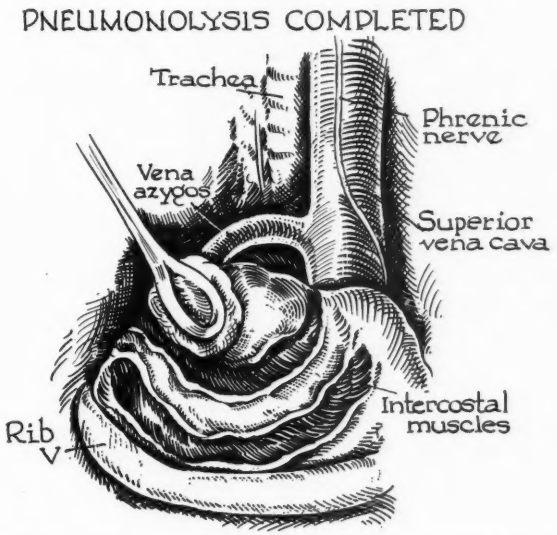

Fig. 2.—Technique of Paulino procedure. Pneumonolysis is completed to the hilum of the right lung.

of the grossly diseased portions of the lung have been uniformly and concentrically collapsed and compressed under direct vision in a far more accurate and dependable manner than is possible by rib resection alone. It should be emphasized that the degree of collapse of the lung is *not* dependent on the extent of the rib resection.

Laceration of the pleura does not unduly complicate the procedure. If the lung is not adherent to the parietal pleura care must be taken that the lung does not slip out as the ligatures are applied. A catheter may be introduced into the pleural cavity and either withdrawn at the close of the opera-

tion as the lung is expanded by the anesthetist, or it may be connected with a water trap for postoperative drainage. The wound is closed in layers with interrupted sutures of quilting cotton. A simple dressing is applied with a small pad placed in the anterior costal defect. The tendency toward paradoxical motion of the chest wall is slight.

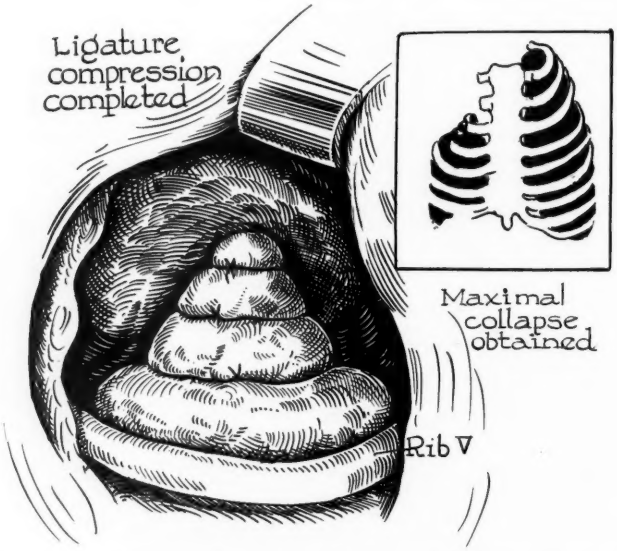

Fig. 3.—Technique of Paulino procedure. Ligature compression completed with demonstration of the maximal collapse obtained.

ADVANTAGES

The chief advantages of this procedure over the Alexander operation are: 1. Deformity is minimized. 2. There is maximal preservation of respiratory function. 3. It is performed in a single stage. 4. There is suggestive evidence that because of the more accurate application of collapse and compression better control of the tuberculosis is obtained. 5. It is applicable to bilateral disease.

INDICATIONS

The general indications for the operation are the same as for the standard type of thoracoplasty, and it may be elected in preference to the older procedure. Special indications for the Paulino procedure are: (1) the presence of bilateral advanced upper lobe disease, (2) the occurrence of unilateral upper lobe disease in a patient who has previously had contralateral thoracoplasty or lobectomy, (3) paramediastinal cavitary disease, (4) unilateral disease in the presence of limited respiratory reserve, and (5) a particular desire to avoid deformity as in a young individual.

CONTRAINDICATIONS

The general contraindications are the same as for the standard type of thoracoplasty. The special contraindications are: (1) the presence of advanced disease below the level of the hilum, (2) a large subpleural cavity, or (3) pleural disease. Ligature compression cannot be effectively applied below the level of the hilum but we have successfully controlled cavitary lesions in the dorsal division of the lower lobe. If absolutely necessary the lowest ligature may be placed on a bias to encompass posterior lesions lying slightly below the level of the hilum. Although we fear complications from ligature compression of a large subpleural cavity, the first patient upon whom we performed the procedure (J. M.) had a 6 cm. subpleural cavity which was successfully closed without untoward incident (Fig. 7, *A* and *B*), but we do not recommend the operation under these circumstances if alternative procedures are available.

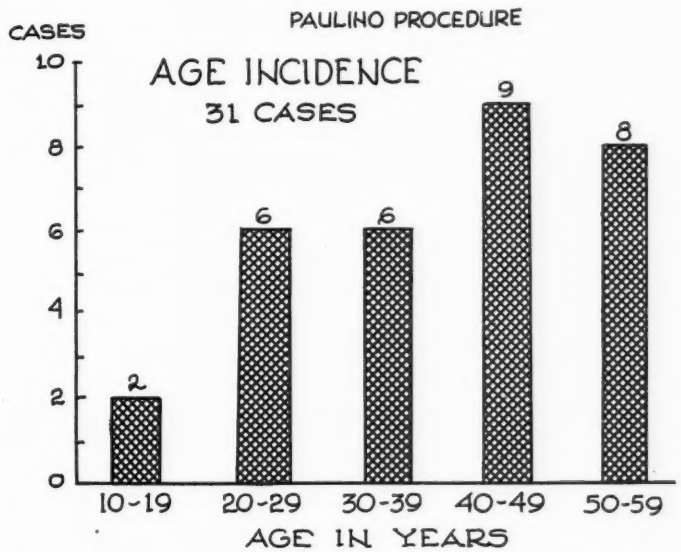

Fig. 4.—The age incidence by decades in thirty-one cases subjected to the Paulino procedure.

OPERATIVE EXPERIENCE

Thirty-four operations have been performed on thirty-one patients.* Of these twenty-eight were white, and three were nonwhite; twenty-three were men and eight were women. The age distribution of the cases is indicated in Fig. 4. Nine patients were in the fifth decade and 8 in the sixth, or a total of seventeen (55%) were more than 40 years of age. The three bilateral operations were performed in patients 28, 52, and 56 years of age.

*Twenty-three operations were performed at the Charity Hospital of Louisiana in New Orleans, seven at the Foundation Hospital, New Orleans, and one at the Mississippi State Sanatorium, Sanatorium, Miss.

The disease was unilateral in four cases, bilateral in twenty-seven, moderately advanced* in five, and far advanced* in twenty-six (Fig. 5). It is to be noted that as a group these cases represent advanced lesions for which either a major resection or an extensive thoracoplasty would have been required had this procedure not been used. On the operative side alone the disease was classified as moderately advanced in twenty-four and far advanced in ten.

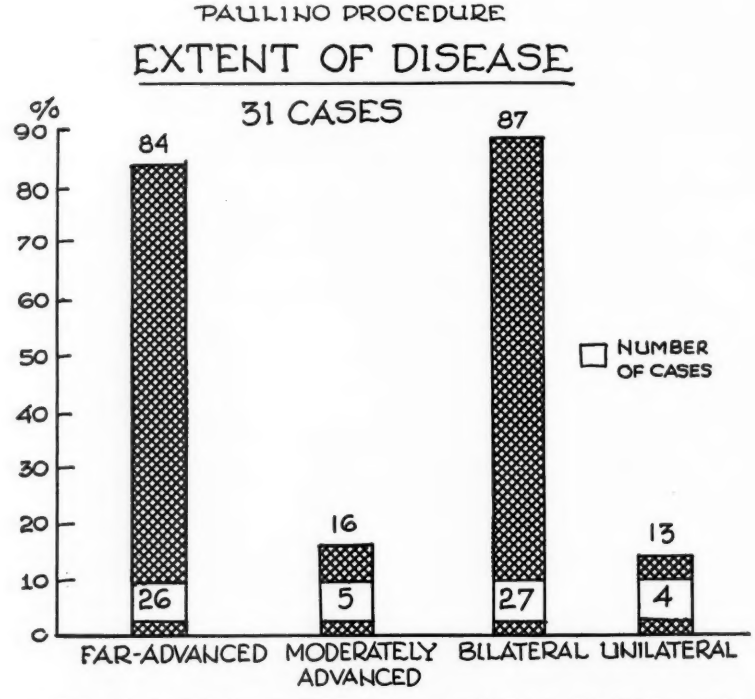

Fig. 5.—The extent of disease in thirty-one cases subjected to the Paulino procedure.

The Paulino procedure was chosen electively on general indications for thoracoplasty in thirteen cases, and on special indications for this technique in eighteen (Table I).

COMPLICATIONS

Serious complications of the operation have been infrequent (Table II). There has been no instance of bronchial fistula or of tuberculous infection of the pleural or extrapleural spaces. There has been no evidence of any of the ligatures cutting through, nor has there been any evidence of interference with the blood supply to the collapsed lung. The margin of safety between adequate collapse and interference with vascularity must be considerable be-

*National Tuberculosis Association Classification of 1950 is used throughout this report.

TABLE I. INDICATIONS FOR OPERATION IN THIRTY-ONE CASES

General indications	13 cases	
Special indications	18 cases	
Possible bilateral operation		7
Probable bilateral operation		6
Preservation of marginal function		6
Prevent deformity		1

cause the thirty-four operations have been performed by seven different operators, including five house officers. The pleura has been lacerated during dissection on eighteen occasions. This occurred more frequently early in the series when the extrapleural dissection was begun inferiorly rather than at the apex. The accident occurs most commonly through the very thin anterior pleura. Extrapleural fluid developed postoperatively in all cases. In eight patients the fluid had to be aspirated more than once and was considered excessive. Intrapleural fluid requiring aspiration developed in seven cases. Subcutaneous emphysema of moderate extent occurred twice. Nontuberculous infection of the extrapleural space developed twice, and of the intrapleural space once. In each instance it responded to simple open drainage.

TABLE II. POSTOPERATIVE COMPLICATIONS FOLLOWING THIRTY-FOUR OPERATIONS

COMPLICATION	CASES
Excess extrapleural fluid	8
Intrapleural fluid	7
Subcutaneous emphysema	2
Infection of extrapleural space	2
Empyema	1
Pulmonary embolism*	1
Respiratory failure*	1

*Fatality.

Two serious hemorrhages have occurred several months following operation. One patient (Case 10, M. L.) died of a sudden massive pulmonary hemorrhage five months after operation. Immediately after operation, a large contralateral paramediastinal cavity became apparent and remained open. The disease on the operative side appeared to be under control. The patient died at home and an autopsy was not performed. It was felt that the hemorrhage occurred in the large contralateral cavity. S. T. (Case 9) experienced severe pulmonary hemorrhage in April, 1951, five months after a left Paulino thoracoplasty and eight months after a similar operation on the right side. The disease was very extensive in both lungs, and it was felt that the collapse obtained at the first operation was technically not quite adequate (Fig. 8, *A* and *B*). This was the first operation performed by that operator. Although spread occurred in the right lower lobe following the hemorrhage, subsequently the disease has become inactive for eight months, and the patient has returned home (Fig. 8, *C*).

In Case 19 (F. H.) ipsilateral postoperative spread occurred. Bilateral apical cavitary disease was present and had not responded to prolonged bed rest with pneumoperitoneum. Either during operation or in the first few postoperative days, which were complicated by transient atelectasis and excessive

extrapleural fluid, the cavity slipped down below the lowest ligature. Subsequently a spread appeared in the ipsilateral lower lobe. This case constitutes a failure of the procedure although the patient has subsequently improved on further conservative treatment.

Two early postoperative deaths occurred. W. C. (Case 8) was ill-advisedly selected for operation as a heroic procedure in spite of very far-advanced bilateral disease extending below the hilum, and a limited respiratory reserve. Although his postoperative course was not otherwise complicated he died on the eighth postoperative day of respiratory failure. D. S. (Case 12) with far-advanced bilateral disease died of an apparent massive pulmonary embolism on the fourteenth day following the second of bilateral Paulino procedures. The disease had apparently been controlled on the first side and the sputum had converted, but a persistent cavity on the second side indicated the second operation. The one late postoperative death, from hemorrhage in the fifth month, has been referred to previously.

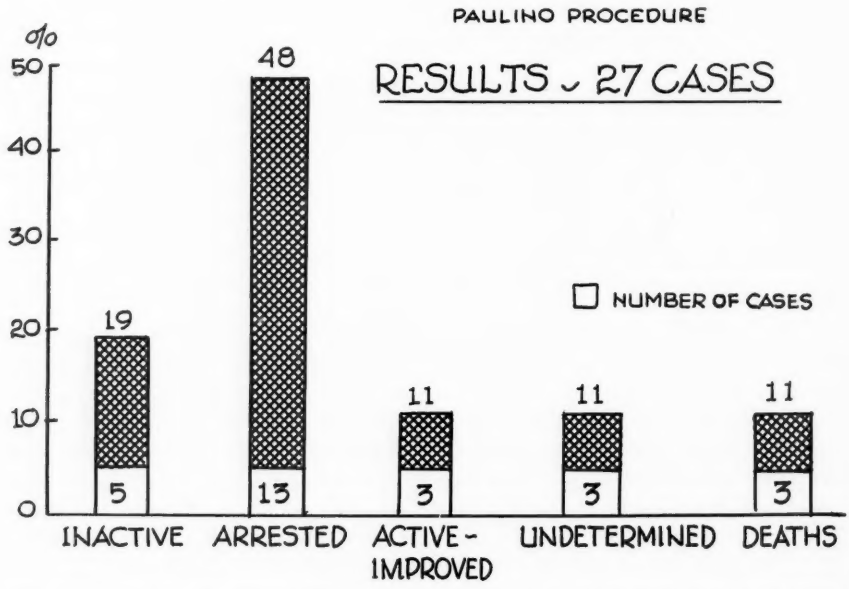

Fig. 6.—Results of the Paulino procedure in twenty-seven cases operated upon more than seven months ago.

RESULTS

Four of the thirty-four operations have been performed in the last four months. In each case adequate collapse has apparently been obtained and the patient is improved, but it is too early to evaluate the results. Two patients have been lost to follow-up. Of the remaining twenty-five patients, who were operated upon more than seven months ago, the disease has become *inactive* in five for periods of 6, 8, 18, 18, and 22 months (Fig. 6). The activity classifica-

tion is unlimited in three, class IV in one, and class III in one. The disease has been *arrested* in thirteen additional cases for 4.5 to 24 months with an average duration of arrest of 12.3 months. In nine of these cases sputum cultures are negative, and in only one case has there been a positive culture (one positive,

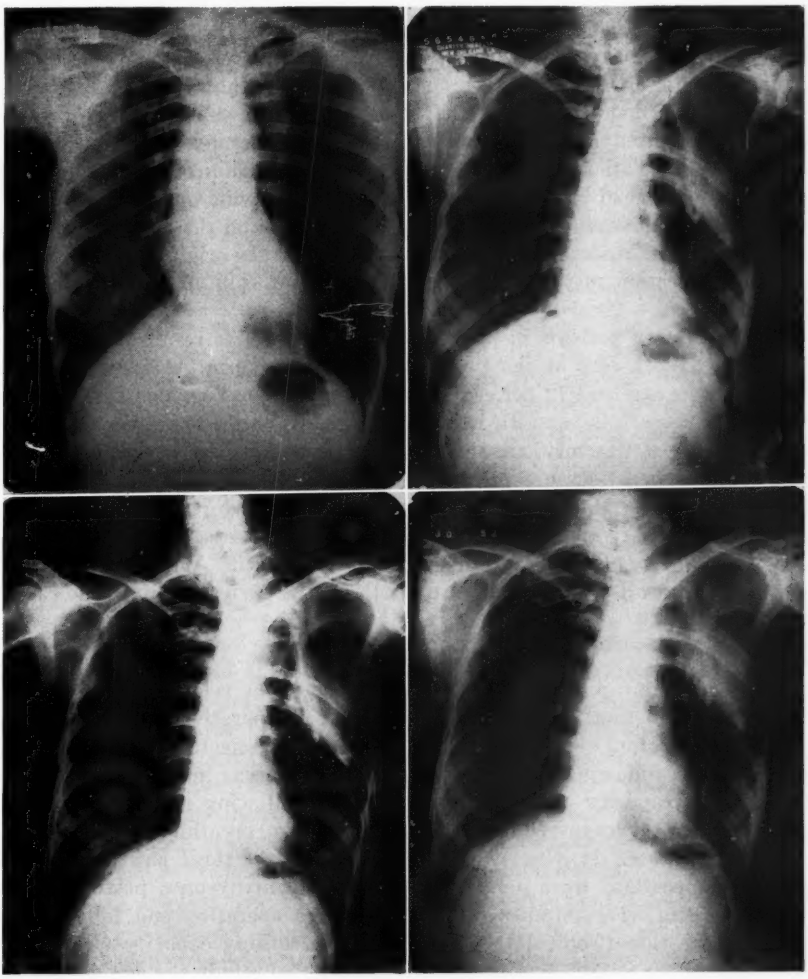

Fig. 7.—Case 1. J. M., a white woman, aged 36 years, with far-advanced bilateral tuberculosis. *A*, July, 1949, a large cavity in left upper lobe. Unsuccessful pneumothorax. Inactive contralateral disease. Left Paulino performed September, 1949. *B*, July, 1951, inactive status, 1 year. Moderate scoliosis. *C*, October, 1951, reactivation and cavitation in right upper lobe. Lesions on left side inactive. *D*, January, 1952, cavity closing on conservative treatment.

two negative) at the most recent checkup. The activity is unlimited in four, and class IV in nine cases. One patient (Case 26) who had negative sputum cultures and no clinical or x-ray evidence of activity on a single postoperative checkup four months after operation is classified, with the two patients who have not been followed, as activity undetermined (Fig. 6).

Three cases are classified as active, improved. The disease in Case 1 (J. M.) became inactive following an operation in September, 1949, and the patient returned to full activity. Two years later contralateral disease reactivated and a cavity formed (Fig. 7, *C*). This is responding to conservative treatment (Fig. 7, *D*). Roentgen studies, including planigraphy, fail to reveal activity on the operative side. F. H. (Case 19) is classified as active; the disease has improved on postoperative conservative therapy but, as previously described, this patient represents the one technical failure of the operation. F. B. (Case 27) had bilateral cavitary disease. Following operation in September, 1951, the disease has apparently been controlled on the operative side and the contralateral disease has improved so much that the originally contemplated bilateral operation may not be necessary. Recent sputum concentrates were negative.

The eighteen patients in whom arrested and inactive results were observed represent 67 per cent of the twenty-seven patients operated upon more than seven months ago, and 72 per cent of the twenty-five cases which have been followed. If Cases 1, 26, and 27, in which the results on the operative side appear to be entirely satisfactory, are added the operation has been beneficial to 78 per cent of the twenty-seven patients operated upon, and to 84 per cent of the twenty-five cases followed. Seven of these patients have returned to full activity. The two early postoperative deaths represent a case fatality rate of 6.4 per cent and an operative mortality rate of 5.9 per cent. With the third (late) death the over-all case fatality rate for the entire series of thirty-one cases is 9.7 per cent.

RESPIRATORY FUNCTION

An important advantage of this operation is the relative preservation of respiratory function. This was borne out by preoperative and postoperative total lung function studies carried out in twelve unselected cases (Table III). In ten cases following unilateral operation there was an average reduction in the vital capacity of 357 ml. In six cases following unilateral operation there was an average reduction in the maximum breathing capacity of 8.7 liters per minute. It is noteworthy that none of the three patients on whom bilateral operations were performed had significant dyspnea postoperatively. In the two in whom studies were made before operation and following the second operation (Table III) the maximum breathing capacity was reduced by 13 liters per minute in one, and 23 liters per minute in the second; and the vital capacity by 290 ml. in one, and 1,280 ml. in the other. Both of these patients have returned to normal activities without significant dyspnea.

ROENTGEN STUDIES

Careful roentgenologic studies in the follow-up period have failed to reveal the persistence of cavitation on the operated side in any case other than

TABLE III. PREOPERATIVE AND POSTOPERATIVE RESPIRATORY FUNCTION STUDIES

CASE	VITAL CAPACITY (ML.)			MAXIMUM BREATHING CAPACITY (LITERS/MINUTE)		
	PREOP.	POSTOP.	CHANGE	PREOP.	POSTOP.	CHANGE
			Unilateral Operation			
1	2,650	2,590	-60	--	90	--
2	1,985	1,550	-435	64	44	-20
3	1,490*	1,270*	-220	--	--	--
5	2,220	1,790	-430	60	49	-11
6	3,230	3,200	-30	99	88	-11
7	2,100	1,905	-195	--	72	--
11	4,060	3,420	-640	--	93	--
12a	3,000	2,460	-540	96	86	-10
22	1,640	1,410	-230	47	53	+6
27	3,070	2,280	-790	75	59	-16
	Mean		-357			-8.7
			Bilateral Operations			
9a	3,560	1,930	--	76	53	--
9b	--	2,280	-1,280	--	53	-23
15a, b	3,670	3,380	-290	104	91	-13

*Contralateral pneumothorax.

a—Indicates patient later had another operation.

b—Represents those patients in whom studies were made before the operation and following the second operation.

Case 19, previously mentioned, where the lung slipped out from under the ligatures. Studies have routinely included erect posteroanterior, lateral, and oblique views, Bucky films, and in nine instances, body section films. Significant scoliosis has developed in only one case (Fig. 7). In a few instances some confusion arose because the lung below the level of the collapse expanded upward, surrounding the collapsed tissues, and giving highlights suggesting cavitation (Fig. 9, *C* and *D*). The differentiation was readily made on study of lateral views and planigrams. Our first case, and two bilateral cases, are represented in Figs. 7, 8, 9.

DISCUSSION

It appears certain that until more effective conservative treatment is developed and all cases of tuberculosis are diagnosed and treated before destructive lesions have occurred, surgery will be called upon to assist in the control of the more advanced pulmonary lesions. Excision of such lesions is theoretically to be preferred to thoracoplasty, but in our experience excision has carried a higher mortality and a higher incidence of serious postoperative tuberculous complications.[3] Therefore we consider thoracoplasty indicated if it can be reasonably expected to control the lesions.

We have a great deal of respect for the multistaged, selective thoracoplasty of the Alexander type,[1, 2] which has proved to be effective, relatively safe, and largely free of serious postoperative complications. The procedure does have, however, several disadvantages. These are: 1. Multiple stages are required. 2. The procedure is frequently deforming. 3. A minimum of six ribs must be removed for adequate collapse. 4. To obtain satisfactory collapse of diseased portions of the lung it is necessary to remove two or more ribs below the level of the lesions thus causing considerable additional loss of pulmonary function. 5. The procedure can seldom be applied to bilateral dis-

ease or to contralateral lesions following lobectomy. 6. In spite of apparently adequate collapse, cavities in the operative area may remain open and the disease become active. It is debatable whether this persistent activity is due to technical inadequacy in the application of collapse and compression, or to inherent inadequacies in the principle of collapse therapy.

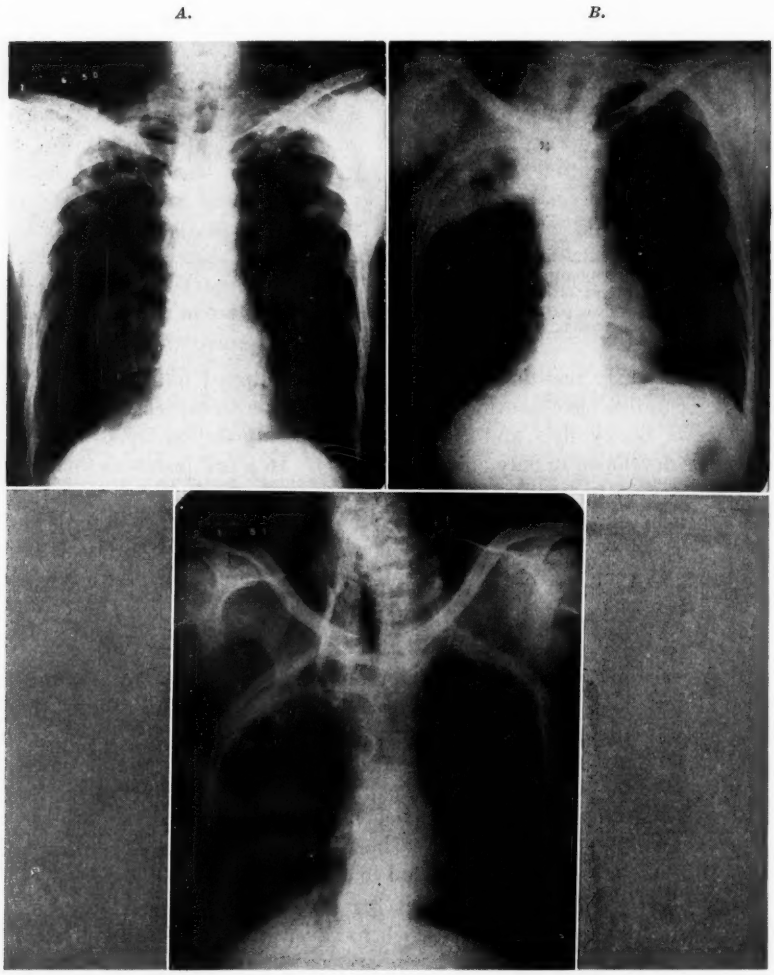

Fig. 8.—Case 9. S. T., a white man, aged 56 years, with far-advanced bilateral pulmonary tuberculosis. *A*, July, 1950, extensive cavitary disease in both upper lobes. Right Paulino procedure performed July, 1950. *B*, September, 1950, appearance following operation. Collapse may have been inadequate. Left Paulino procedure October, 1950. *C*, October, 1951, hemorrhage and right lower lobe spread in March, 1951. Subsequent response to antibacterial therapy. Disease inactive in April, 1952.

Numerous attempts have been made to modify, or to substitute for, this procedure in an effort to avoid these disadvantages. Partial thoracoplasty, extrapleural pneumonolysis with or without plombage, or a combination of the two procedures as in the Semb operation do indeed avoid many of these disadvantages. They have uniformly failed, however, in the most important

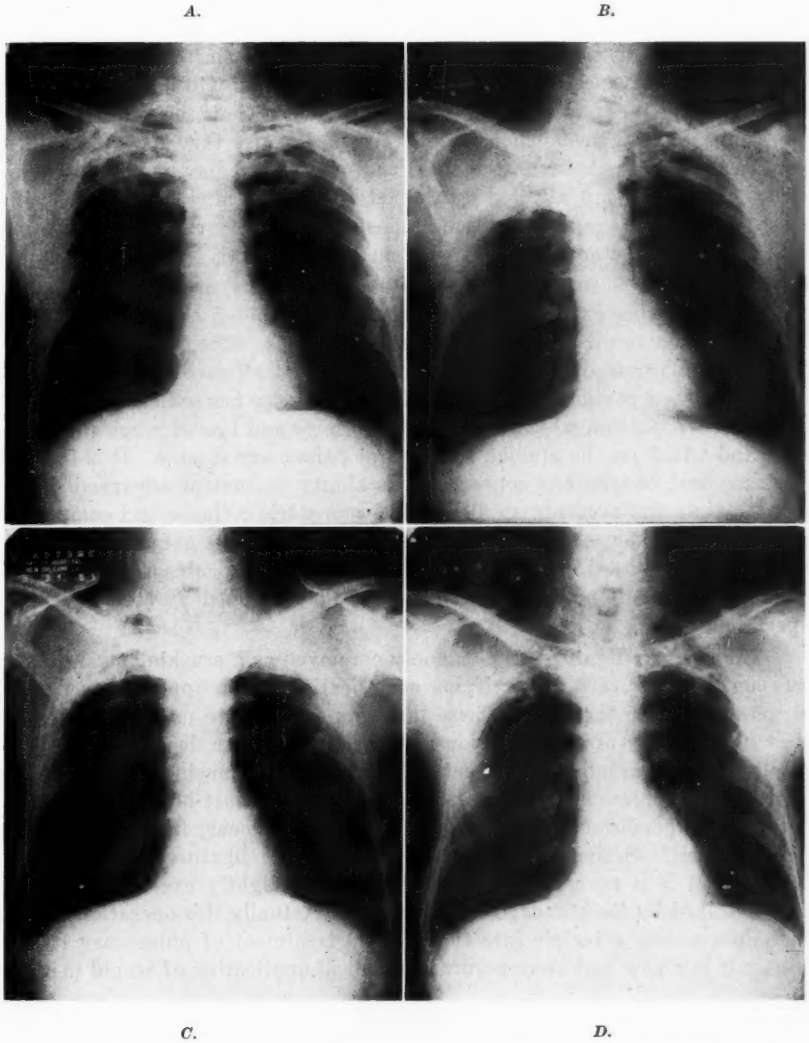

Fig. 9.—Case 15. L. B., a white man, aged 52 years, with far-advanced bilateral tuberculosis. *A*, December, 1950, extensive bilateral cavitary disease. Right Paulino procedure, December, 1950. *B*, April, 1951, good collapse of operative side. Persistent contralateral disease. Left Paulino procedure, April, 1951. *C*, May, 1951, good bilateral collapse. *D*, October, 1951, some overexpansion of lungs below the collapse causing highlighting which may be mistaken for cavities.

attribute of the Alexander operation and that is the control of advanced cavitary lesions in a high percentage of properly selected cases. We feel that these procedures fail either because of inadequate collapse or, even if the collapse is "adequate," because sole reliance is placed on the inherent ability of the diseased tissues to contract and to "control" themselves. The experience with intrapleural pneumothorax, extrapleural pneumonolysis, and partial thoracoplasty has amply demonstrated that if reliance is placed simply on the collapse of the diseased tissues onto the underlying elastic and mobile pulmonary tissue advanced destructive lesions of the lung will be controlled only sporadically. We feel that an important reason that the more extensive thoracoplasties are so much more effective is because they fix and compress the diseased tissues between the chest wall and the mediastinum, and the collapsed tissues are not affected by the activity of the lung below the level of the collapse. No one who has done a postthoracoplasty resection of the lung can doubt the factor of compression in an adequately performed thoracoplasty.

We tried this procedure chiefly because it avoided the pitfall of inadequacy common to all other conservative operations. The diseased tissues are collapsed, compressed, and fixed, and they are not affected by the activity of the uncollapsed portion of the lung. Our experience has indicated that it is a safe, single operation which minimizes deformity and loss of respiratory function, and which can be applied to bilateral pulmonary disease. It is too early to draw final conclusions concerning its ability to control advanced disease, but certainly the accurate application of concentric collapse and compression under direct vision should be as effective as the results obtained blindly by removal of the costal cage. Our experience to date indicates that the collapse is as effective as, if not more effective than, that obtained by the more radical operation.

The use of a ligature, so commonly employed as a crushing strangulating weapon, suggests certain horrifying complications when applied to a vascular structure such as the lung. These thoughts occurred to us, and we are sure that if the safety of the operation had not already been demonstrated by Dr. Paulino we would have been reluctant to try it. The margin of safety between adequate compression and dangerous strangulation must be great as the procedure was performed in our series by seven surgeons, five of whom were house officers. Serious troubles could arise if the ligatures were carelessly applied but it is necessary only to equal, or to slightly excell, the compression obtained by the standard thoracoplasty. Actually this operation does not introduce a new principle into the surgical treatment of pulmonary tuberculosis. It is a new and more accurate technical application of an old principle.

SUMMARY

A technique of partial thoracoplasty, extensive pneumonolysis, and collapse and compression of the lung by suture ligatures is presented. A thirty-one-month experience in thirty-one cases, including bilateral operation in three cases, indicates that this procedure is safe and reliable when applied to suitable

advanced tuberculous lesions of the upper lung. The operation is performed in one stage; costal resection, deformity, and loss of respiratory function are reduced to a minimum; and it has been applied successfully to bilateral disease.

The procedure is recommended particularly when bilateral surgical procedures seem indicated, or when the respiratory reserve is limited. As the operation has several additional advantages it may also be used by election rather than the more extensive multistaged selective thoracoplasty of the Alexander type.

REFERENCES

1. Alexander, John: Special Considerations Relating to Surgical Closure of Large Upper Lobe Tuberculous Cavities, J. THORACIC SURG. **2**: 1-23, 1932.
2. Alexander, John: The Collapse Therapy of Pumonary Tuberculosis, Springfield, Ill., 1937, Charles C Thomas, chap. 23, pp. 450-493.
3. Baffes, Thomas G., and Schlotterbeck, Phyllis: Unpublished observations, April, 1952.
4. Paulino, Fernando: Toracoplastia com apicolise total e amarracao de pulmao, Rev. med.-cir. do Brasil. **56**: 7-12, 1948.
5. Paulino, Fernando: Thoracoplastic Avec Apicolise Totale Et Ligature Du Sommet Du Pulmon, rapport aux "Giornate Mediche Internazionale." Verona, Italia, July 28-31, 1949.
6. Semb, Carl: Thoracoplasty with Extrafascial Apicolysis, Acta chir. Scandinav. (Supp 37b) **76**: 1-85, 1935.

CLINICAL EXPERIENCE WITH THE WATER-SOLUBLE BRONCHOGRAPHY COMPOUNDS

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THE use of absorbable water-soluble contrast solutions for bronchography has attracted considerable attention in recent months. In fact, five different drug concerns have made products of this type commercially available for routine or investigational use. Sufficient individual clinical experience has not yet been gained to evaluate these compounds adequately. Consequently, it seems advisable to review the products available, to correlate some of the experience which has been gained, and to emphasize some serious complications which have resulted from their use.

The proprietary products now available do not vary significantly in their physiologic activity. They do vary, however, with regard to their chemical composition. All have as their contrast medium iodopyracet (the diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid) or a very closely related product. This material has for a number of years been marketed in this country as Diodrast.* It has been extensively used for intravenous urography and angiography, and its properties are well known. In 1948 Morales and Heiwinkle[1] described experimental and clinical studies with a combination of 35 per cent iodopyracet in 2.5 per cent carboxymethylcellulose (the sodium salt of cellulose ether). This material is now marketed by Astra under the trade name of Umbradil Viscous B. The product is a slightly viscous solution, about 500 centipoise (cps.), and does not have a consistency which would seem ideal for bronchography. However, very excellent bronchograms have been obtained with this material, as is attested by the recent reports of Atwell and Pedersen,[2] Filpse, Hedberg, and Krueger,[3] and others.[4]

Per-Abrodil "M," marketed by Bayer as Per-Abrodil "BP," is an identical product but with a viscosity adjusted to 3,500 to 4,000 cps. at 37° C. Reference will subsequently be made to the extensive work done in Germany with this substance.[5]

Two other available products, Ioduron B (Cilag)[6, 7] and Diodone Visquese (Guerbet),[8] have approximately the same concentration of iodine per cubic centimeter[3] (0.25 Gm.). The base in these compounds, glycolmethyl cellulose, results in a solution of much greater viscosity. Diodone (4,000 cps.) is rather jellylike in consistency and has a slight brownish discoloration. Ioduron (35,000 to 40,000 cps. in 2.5 per cent solution) is highly viscous, tends to precipitate crystals which redissolve on warming, and also has the brown color. We

Read (by title) at the Thirty-second Annual Meeting of The American Association for Thoracic Surgery at Dallas, Texas, May 8-10, 1952.

From the Department of Surgery (Division of Thoracic Surgery) and the Department of Radiology, University of Colorado Medical Center.

*Manufactured by Winthrop-Stearns, Inc.

have on various occasions attempted to identify free iodine as the cause for the discoloration in these two products but have been unable to do so.

The fifth product we have originally described as Methocel-Diodrast.[9, 10] It is now available for investigational use through Winthrop-Stearns, Inc. This material is composed of 50 per cent Diodrast in 1.75 per cent methylcellulose. It forms a clear, relatively viscous solution which compares in consistency with the iodized oils. Pure methylcellulose (4,000 cps.) was chosen for this particular product because of the extensive studies which have been carried out indicating that it is essentially nontoxic.[11-13] The majority of all our bronchograms performed to the present time have been made with contrast media compounded with pure methylcellulose. We have occasionally used a product prepared with carboxymethylcellulose but have felt that the degree of bronchospasm which accompanies its introduction is somewhat greater than with methylcellulose solution. It appears that the efficiency of carboxymethylcellulose, methylcellulose, and glycolmethylcellulose as thickening agents increases in this order at similar concentrations. We feel, therefore, that this irritative response is not due to the carboxymethylcellulose but rather to the lower viscosity of the carboxymethylcellulose solutions tried. This low viscosity allows for a more rapid absorption of the iodopyracet.

We have reviewed our first fifty-six bronchograms made with water-soluble media (Methocel-Diodrast in all instances) for the purpose of determining whether the technique, the contrast, and the bronchial filling were of such quality as to be consistent with a satisfactory bronchogram. Of these fifty-six cases, twelve were considered unsatisfactory. Seven resulted in a division of opinion, and thirty-seven were considered unquestionably satisfactory. Because of the division of opinion the seven questionable bronchograms were classified as unsatisfactory. This means that 66.7 per cent of the bronchograms reviewed were satisfactory and 33.3 per cent were unsatisfactory. Correspondence with others who have been using the water-soluble materials in this country has given us eighty-three added reports on their use. These reports indicated a marked division of opinion concerning the results obtained with these agents. Those who were enthusiastic with their use obtained satisfactory bronchograms, whereas those with a limited experience in their use obtained unsatisfactory bronchograms. In general, approximately one-third of the studies which were reported were considered unsatisfactory. This corresponds with our observations.

There are many factors which contribute to the success or failure of bronchography, even with such standard solutions as Lipiodol and Iodochloral. Therefore, it is essential that these results be compared with another series in which the iodized oils were used. One of us (A. J. N.) was, during military service, Chief of the Peroral Endoscopy Section in a large army hospital. During that time a record was kept of bronchograms performed and of the number which were unsatisfactory. A total of 528 bronchograms were made using Lipiodol, and of these 83 were unsatisfactory. This gives a percentage of 15.9 unsatisfactory bronchograms. It would seem, therefore, that it is possible to

obtain a satisfactory bronchogram more consistently with one of the nonabsorbable iodized oils. On the other hand, enthusiasm for the water-soluble media is somewhat greater among our European colleagues. Dr. Karl-Heinz Willmann reports on over 2,000 bronchograms with Per-Abrodil "M" 60 per cent Viscous, done for all kinds of pulmonary disease.[14] The large majority of these bronchograms were considered satisfactory and no untoward results were observed.

The explanation for the discrepancy between the results obtained with water-soluble and oil contrast media rests in a number of factors which are inherent in any of the water-soluble media presently available. First, the absorption of the contrast material, in all instances iodopyracet, is extremely rapid. Hence, to obtain results which are at all satisfactory it is necessary to become familiar with the use of these media. Second, the material is miscible with the bronchial secretions and, consequently, it tends to fill the peripheral bronchial tree confluently. This is in contrast to the picture with iodized oils in which the bronchial tree is outlined and "clubbing," due to blockage by retained secretions, is observed. (See Fig. 2 for this comparison.) One must, therefore, learn to read these bronchograms from a somewhat different point of view than is the case with the iodized oil. Third, and perhaps most significant, is the fact that these media tend to create a rather severe degree of bronchospasm.* This, of course, contributed considerably to the "unsatisfactory" group of films, as manifested by incomplete filling secondary to the explosive effect of coughing. Elimination of coughing is essential to satisfactory bronchography. This is a good deal more difficult to obtain with iodopyracet compounds as the bronchographic agent than with iodized oil. However, meticulous attention to the topical anesthetization of the tracheobronchial mucosa will improve the results when using a water-soluble agent. It is interesting that this response is not as marked in the individual with diseased bronchi as in the case of the individual with the more normal bronchial tree. We also feel that the bronchospasm is somewhat greater where the products utilize carboxymethylcellulose as a base because the viscosity is so low that the iodopyracet is more rapidly absorbed from the bronchioles and alveoli. This statement hypothesizes that the iodopyracet is the factor which leads to bronchospasm. The explanation is thought to be related to a reflex mechanism precipitated by rapid absorption, through a tremendous vascular bed, of a large amount of iodopyracet in a very short period of time. On several occasions we have seen a degree of irritation which exceeded mere coughing and resulted in a profound degree of bronchospasm and laryngospasm, even requiring intubation to maintain an airway. Suggestive evidence that iodopyracet is the stimulating factor is given by the observance of similar severe bronchospasm in a patient who died following the rapid intravascular injection of iodopyracet for angiocardiography.

The use of water-soluble media may also carry the danger of leading to a fatality. We have had two deaths associated with bronchography in which these materials were used. These cases should be reviewed at this time.

*Note: We have not proved that the cough, as clinical evidence of bronchial irritation, is secondary to bronchospasm but are assuming that this is true.

CASE REPORTS

CASE 1.—L. S., a white woman, 53 years of age, was admitted to Denver General Hospital on May 12, 1951, because of cough, weakness, and loss of weight. She also reported exertional dyspnea and small amounts of frothy yellow sputum. No allergic history was elicited.

On physical examination blood pressure was 110/60, pulse 120, and temperature 100.2° F. Auscultation of the chest revealed dry inspiratory and expiratory râles throughout both lung fields. Dullness was present in the right base posteriorly. The heart was enlarged to the left. Circulation time, arm to tongue, was 13 seconds, and the venous pressure was 70 mm. of water. Admission laboratory work was not remarkable aside from a white blood count of 11,400. X-ray examination of the chest showed a questionable enlargement of the right hilar area. Sputum was repeatedly negative for acid-fast bacilli. Bronchoscopy performed under topical cocaine anesthesia was negative.

On June 6, 1951, the patient was prepared for bronchography. She was given atropine 6 mg. on the ward and 50 mg. of Seconal Sodium intravenously upon arrival in the operating room. The pharynx and larynx were topically anesthetized with 20 c.c. of 5 per cent cocaine hydrochloride solution. A No. 14 French catheter was inserted into the trachea. Two cubic centimeters of 5 per cent cocaine solution was injected into both right and left main stem bronchi through the catheter. The patient was then taken to the x-ray department. Her condition appeared satisfactory. An intracutaneous test (0.1 c.c.) for sensitivity to Diodrast was negative. Fifteen cubic centimeters of 50 per cent Diodrast in 1.75 per cent methylcellulose was then instilled into the right bronchial tree. The patient was positioned and roentgenograms were taken. Fifteen cubic centimeters of the same material was then injected through the catheter into the left bronchial tree and the patient positioned. As the x-ray films were being taken the patient lost consciousness and had a convulsion. She was immediately returned to the operating room, where the pharynx was cleared of a small amount of the material and an endotracheal tube was inserted. At this time the patient had a second convulsion. Subsequently, respiratory motions ceased. She was given .5 Gm. of caffeine intravenously, and artificial respiration was maintained with oxygen under positive pressure from an anesthetic machine. Shortly afterward the heart beat became gradually weaker, and the patient was pronounced dead approximately thirty minutes after the initial convulsion.

The significant post-mortem findings were confined to the lungs, which both showed pulmonary edema, emphysema, and gross focal hyperemia. The report of the microscopic examination follows: The lungs showed focal areas of recent hemorrhage, in which the air spaces are packed with red blood cells. The septa were delicate, and the capillary spaces were filled with red blood cells, neutrophils, and eosinophils. The mucosa of the bronchi and bronchioles was intact. The submucosa was diffusely infiltrated with eosinophils and an occasional lymphocyte and mononuclear cell. In focal areas there was scattered a slight amount of anthracotic pigment. The kidneys revealed focal collections of eosinphils within the capillary spaces of the glomeruli. A Sudan fat stain of the adrenals revealed a normal component of fat. Sections of heart, liver, spleen, pancreas, adrenals, and brain revealed hyperemia but no other significant lesions.

Comment.—The pathologic summary* was as follows: "The finding of marked eosinophilia in the lungs was consistent with acute anaphylactic shock. Eosinophilic neutrophil infiltration of viscera has been described in acute adrenal insufficiency. However, this can probably be excluded by the demonstration of a normal fat component in the adrenals.

"Four volunteers, including myself, were used in an attempt to demonstrate a Prausnitz-Küstner reaction. The areas of skin passively sensitized with the patient's serum were tested with Demerol, cocaine, and the medium

*The post-mortem studies on this patient were conducted by Dr. Joseph R. Kraft, Chief Pathologist, Denver General Hospital.

used in bronchography. Negative results were obtained in each instance. Since passive transfer of drug sensitivity is rarely demonstrable, a negative P-K reaction does not exclude it. Toxicologic examination of vital viscera for cocaine demonstrated only minute amounts, so death due to overdosage, but not to sensitivity, can be excluded.

"Therefore, this is a case of a 53-year-old white woman who came to sudden death during a bronchographic procedure. The autopsy findings exclude to my satisfaction all causes of sudden death except that due to anaphylactic shock. Of the drugs given to the patient, none can be explicitly implicated nor excluded."

Certain clinical factors may also be of some significance in the final evaluation of this patient. She had previously received cocaine topically for bronchoscopy without any evidence of sensitivity, although on the occasion of bronchography she did receive 1.2 Gm. of the drug. Moreover, the time relationship between the last administration of cocaine and the initial convulsion (approximately fifteen minutes) would hardly be consistent with a cocaine reaction. On the other hand, the time relationship between the injection of Methocel-Diodrast and the convulsion (approximately five minutes) is consistent with a reaction to one of the components of this solution. Previous intracutaneous testing for sensitivity to Diodrast, while not conclusive, would tend to free this drug from implication. The evidence at hand, therefore, is suggestive enough to lend suspicion to methylcellulose as the causative factor in the anaphylactic response.

CASE 2.—B. S., a white woman, aged 69 years, was admitted to Colorado General Hospital, Tuberculosis Service, on Oct. 10, 1951, because of a chest survey film which was reported as showing far-advanced pulmonary tuberculosis. She denied all symptomatology and had had no weight loss. Past history revealed that the patient's first husband died of tuberculosis during World War I. The patient then remarried and had lived with her second husband twenty years, during which time she considered herself completely asymptomatic. The family, however, suspected tuberculosis because the patient had a constant chronic cough. No allergic history was elicited.

Physical examination revealed a well-developed individual in no distress. The trachea was deviated to the right. There was dullness to percussion over the medial portion of both lung fields posteriorly. Sputum and gastric washings were examined over a four month period and were consistently negative for acid-fast bacilli. X-ray examination showed a contracted right upper lobe, within which were areas of radiolucency thought to represent cavitation. The mediastinal structures were shifted to the right. Several radiolucent densities, thought also to be cavities, were apparent in the left mid-lung zone near the hilus. Tomograms subsequently confirmed these findings.

First strength P.P.D. was negative. Second strength P.P.D. was faintly positive. Skin tests for histoplasmosis and coccidioidomycosis were negative. Three bronchoscopies were performed with consistently negative results except for the rather marked deviation of the trachea to the right.

The patient's course on the ward was uneventful. She remained afebrile and without complaint. During four months of observation she gained sixteen pounds.

On Feb. 5, 1952 bronchography was performed. The pharynx and larynx were topically anesthetized with 5 per cent cocaine. A No. 16 catheter was introduced through the larynx into the right main stem bronchus. One cubic centimeter of 5 per cent cocaine (total amount of cocaine used was less than 1 Gm.) was introduced through the catheter

for further anesthesia. Fifteen cubic centimeters of 50 per cent Urokon Sodium in 1.75 per cent methylcellulose was then injected into the right main bronchus. The patient did not cough and had no complaints. About ten minutes after the introduction of the contrast medium, and while waiting for the original films to be developed, the patient stated that she wanted to lie down. The patient's color was noted to be bluish-gray, and the pulse was rapid and thready. Almost immediately she became unresponsive and the pulse imperceptible. Subsequently respiration ceased and a frothy foam appeared from her mouth. The mouth and pharynx were aspirated, and intracardiac stimulants were given but were unsuccessful in the face of the marked and rapid circulatory collapse.

Post-mortem examination revealed the trachea and both main bronchi to be filled with bloody mucus. The mucosa of the trachea and right main bronchus showed hyperemia and petechial hemorrhages over an area corresponding to the distribution of the dye on the bronchogram (Fig. 1). The smaller bronchi on the left contained a clear, viscid, mucoid material. The upper lobe of the right lung appeared atelectatic and the bronchi compressed. The middle and lower lobes were red, heavy, and wet. Large portions of the lung parenchyma were replaced by irregular areas of firm gray tissue resistant to cutting.

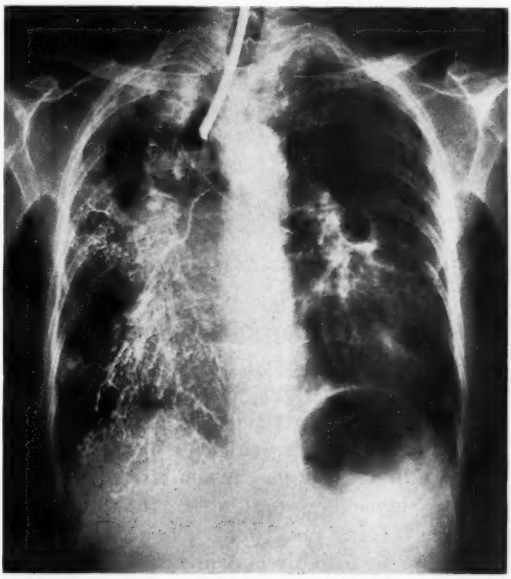


Fig. 1.—Bronchogram of the patient (Case 2) made prior to death in circulatory collapse. The distribution of the medium within the tracheobronchial tree corresponded to the area of mucosal hyperemia and petechial hemorrhage observed at post-mortem examination.

The cavities described by x-ray films had irregular necrotic walls and were filled with purulent exudate. The bronchi of the right lung were edematous and contained petechial hemorrhages in their walls and gross hemorrhage in their lumens. The surrounding lung was very hyperemic and edematous, with areas of frank fresh hemorrhage into the alveoli.

Microscopic examination revealed the cavities to be large bronchiectatic cavities with secondary abscess formation. The remains of the bronchiolar wall could be identified around the abscess. The cavities were filled with segmented neutrophils, and the walls were densely infiltrated with neutrophils and phagocytes. None of the cavities had the appearance of caseation necrosis.

The lesions in the lungs were granulomatous, composed of giant cells, epithelioid cells, a few lymphocytes, macrophages, and areas of fibrosis. The giant cells were atypical, many having central nuclei and containing inclusion bodies. Gömöri stains showed the areas which had been interpreted as necrosis to be actually areas of fibrosis. Intact collagen fibers extended through the lesions. The reticulum stains showed reticulum fibers arranged in whorls around the central giant cells in many of the lesions and merging with the collagen fibers in the fibrotic areas. Tubercle-like lesions, consisting of giant cells, and stellate-arranged epithelioid cells were found in lymph nodes from the neck, chest, and abdomen, in the spleen, and in the myocardium. Circumscribed areas of fibrosis were present in the liver.

The interpretation of these findings led our pathologists to the following conclusions: The cavities seen in the x-ray pictures were actually large bronchiectatic cavities with secondary abscess formation. The granulomatous lesions, when considered in conjunction with the history, laboratory findings, anatomical location, and specific characteristics, were those of sarcoidosis rather than tuberculosis. The clinical picture, the time factor, and the post-mortem findings support the diagnosis of death due to an anaphylactoid reaction to the substance used for bronchographic study.

Comment.—The nature of this patient's death leaves little doubt but that it was caused by an anaphylactoid type of reaction. The distribution of the hemorrhagic reaction within the wall of the tracheobronchial tree, when compared with the bronchogram, certainly implicates the medium which was used for bronchography. Unfortunately, the patient was not previously tested for sensitivity to the Urokon or the methylcellulose. However, the literature now available does not reveal any reports of serious reactions to Urokon. It is being extensively used for urography, and we have been unable to obtain information of any serious unreported reactions. We have been using it in 70 per cent concentrations for aortography and have found it to cause essentially no reactions, vasospasm, or pain, even under local anesthesia. Moreover, experience has shown it to be so rapidly absorbed from the lung that the symptoms of sensitivity to this drug should have appeared much sooner if it were to be related to the reaction observed in this patient. On the other hand, methylcellulose would be expected to be absorbed more slowly. It is primarily disposed of by the lymphoid elements and the reticuloendothelial system. This system was primarily involved, as is evidenced by the areas of hyperemia and actual hemorrhage within the spleen. A similar hyperemia was observed in the liver, and the liver sinusoids were dilated. It seems reasonable to assume, therefore, that death in this instance could be related to the use of the methylcellulose, even though we have no direct evidence in this regard.

DISCUSSION

The concept of a water-soluble agent which will disappear from view shortly after the x-ray examination is especially appealing for tuberculous patients[15] as well as in routine bronchography.[16] Residual iodized oil remaining in the lung is a definite handicap to future study of the pulmonary tree. We feel that the water-soluble agents now available are helpful in overcoming this difficulty (Fig. 2). Nevertheless, they cannot be used without an awareness of the complications and difficulties related to their use. These difficulties might be grouped into three categories: namely, technical, toxic, and latent tissue reactions.

The technical difficulties are primarily associated with the rapidity with which the contrast medium is absorbed. The medium is taken up from the pulmonary tree with such great rapidity that within a few minutes practically none of the contrast substance is visible. Therefore, teamwork is essential between the physician performing the bronchography and the x-ray technicians. It is also almost impossible to fluoroscope these patients during the procedure of bronchography because of this inherent characteristic.

Bronchograms made with these media do not result in as high a degree of contrast as do iodized oils. This may be advantageous to a certain degree, since small parenchymal lesions will not be obscured by the medium. We have, however, made numerous attempts to improve this factor somewhat.

Fig. 2.—The x-ray films demonstrate, on the same patient, the comparison between iodized oils (Lipiodol) and water-soluble medium (Methocel-Diodrast) in bronchography. The film on the left shows a bronchogram of the right chest made with Lipiodol Jan. 12, 1951. On Feb. 27, 1951, a bronchogram of the left chest was made with absorbable contrast medium. The two films are comparable in their demonstration of the bronchial tree, although the Lipiodol gives a more striking contrast. However, the retained oil remains to confuse future evaluation on roentgenogram of the right lung, whereas the left lung was completely clear of the contrast material within a very short time.

Essentially, every water-soluble, radiopaque substance known has been studied.[17] Tetraiodophenolphthalein might seem to be ideal, since it is a compound containing four iodine atoms to the molecule in contrast to the two atoms of iodine in iodopyracet. However, this particular material is not miscible with the high molecular carbohydrate, methylcellulose, which we have been using as a base. This is apparently due to the very considerable difference in pH of the two substances, and it is necessary to choose a substance with a pH approximating that of the body to prevent damage to the tracheobronchial mucosa. A similar situation exists with sodium iodide as it relates to miscibility. Of the barium salts only barium sulfate is nontoxic, but because of its physical properties it is not suitable. Thorotrast might seem to be an ideal substance except that it is not absorbed from the pulmonary parenchyma as are other water-soluble media.[18] Instead, it apparently remains in

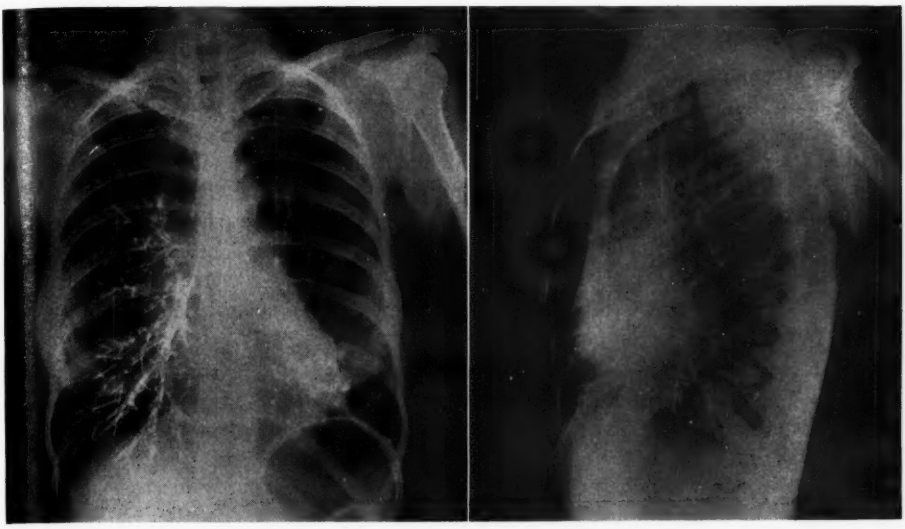
the reticuloendothelial system of the lung. This retention in the face of its mild radioactivity is a disadvantage. Of the remaining substances, Neo-Iopax and Skiodan seem to have no particular advantage over Diodrast. Lately we have been very interested in Urokon Sodium* because of its reportedly low toxic manifestations and because Urokon Sodium contains 65.8 per cent iodine per molecule as compared with 49.8 per cent iodine per molecule in Diodrast.[19-22] Initial bronchograms in human patients using 35 per cent Urokon Sodium in 1.75 per cent methylcellulose have given us the impression that there is a slight improvement in contrast with this particular medium (Figs. 3 and 4). Further studies are being carried out with this substance at the present time. However, it cannot be anticipated as being the final answer because it is absorbed at about the same rate as is iodopyracet.

The toxic manifestations of the water-soluble media add a certain degree of hazard to their use. As we have pointed out earlier, the water-soluble compounds seem to create a marked degree of bronchospasm, particularly in those individuals who do not have a severely diseased bronchial tree. Moreover, it may well be, in certain individuals, that there is a localized allergic response to the high molecular carbohydrate base or to the contrast substance utilized. Evidence is suggestive in this regard but not conclusive.

The severe degree of bronchospasm can often be overcome with adequate anesthetization. It has been our practice to inject about 1 c.c. of 5 per cent cocaine directly into the main stem bronchus of the side to be examined, just prior to the introduction of the bronchographic medium. This has considerably alleviated the degree of bronchospasm elicited in certain individuals. Unfortunately, it does not always prove effective. This method of introducing cocaine directly into the bronchial tree may in itself result in certain hazards. Experimentally it is known that the rapid assimilation of low concentrations of cocaine may be more toxic than slow assimilation of high concentrations of the drug. Death can, therefore, ensue from endobronchial anesthetization in this manner. It is our impression at the present time that Urokon Sodium does not precipitate the bronchospasm observed with the use of iodopyracet. At least, in no instance have we observed any unusual stimulation of the cough reflex when Methocel-Urokon has been used.

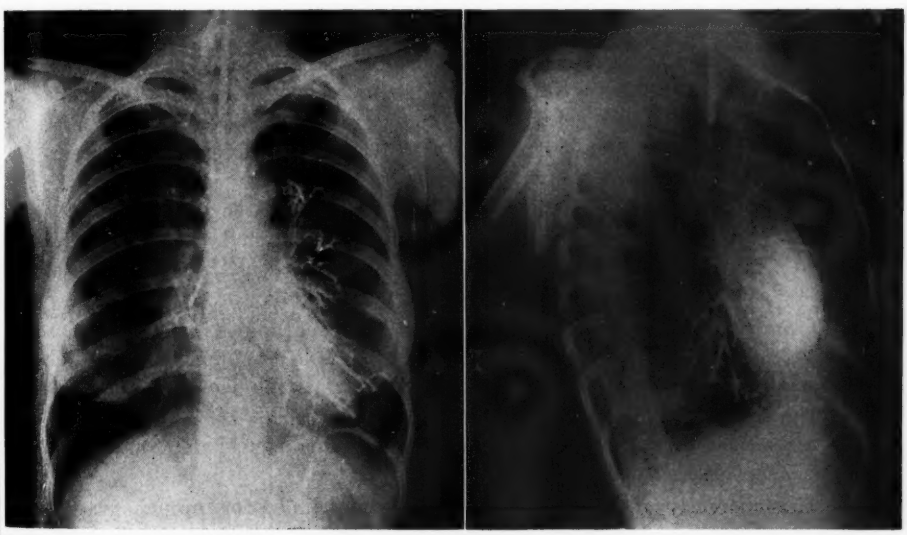
The latent effects of the water-soluble agents upon pulmonary tissue are not clearly understood. Vischer has reported the occurrence of a fibrotic reaction surrounding small foci of carboxymethylcellulose and glycolmethylcellulose which were retained in the pulmonary parenchyma.[23] Experimentally in dogs we were unable to detect any early evidence of an inflammatory reaction or any early evidence for retention of methylcellulose within the pulmonary tissues.[9] However, it is altogether conceivable that these high molecular compounds are retained to some degree within the pulmonary tissue. They are known to be engulfed by the reticuloendothelial cells, particularly in the liver and spleen, when introduced intravenously in large amounts.[11, 12] There is no reason to suppose that they might not be similarly engulfed in the reticu-

*Urokon Sodium is the trade name for sodium 3-acetylamino-2,4,6-triiodobenzoate; it is produced by the Mallinckrodt Chemical Works.



A. *B.*

Fig. 3.—*A* and *B*, Bronchograms illustrating the results which can be obtained with 35 per cent Urokon Sodium in 1.75 per cent methylcellulose. We feel that the contrast obtained on x-ray pictures with this material is superior to other water-soluble media and that the complicating bronchospasm is considerably less. (The films demonstrate clearly bronchiectasis limited to the segments of the left lower lobe and lingula.)



A. *B.*

Fig. 4.—*A* and *B*, See legend for Fig. 3.

loendothelial system of the lung following endobronchial introduction. In fact, Helmström and Holmgren did observe such a response with the endobronchial introduction of carboxymethylcellulose in rats and rabbits.[24] It is improbable, though, that all of this high molecular compound is absorbed. We feel that a great deal of this material is coughed up and expectorated, as is true with the iodized oils.[25] That which remains may act as any substance which is introduced into the bronchopulmonary tree and which is retained; that is, it is likely to give a latent reticular or fibrotic reaction around the retained nidus. This is true after the introduction of Lipiodol,[26, 27] yet it does not seem to be a contraindication to the use of this material. It does not seem to us, therefore, that this fact can be considered a serious deterrent to the use of the water-soluble compounds.

It can justly be said that no compound yet available has all the ideal characteristics for a bronchographic medium. The current water-soluble compounds are a step in the right direction. They must be used with caution and understanding as to their intrinsic dangers and limitations. They are an adjunct in our armamentarium for the diagnosis of pulmonary disease. They are not, however, the final answer and should not preclude further extensive study to find the more ideal agent for use in bronchography.

SUMMARY

The current status of water-soluble absorbable media for bronchography has been reviewed.

The advantages and disadvantages of these media have been enumerated and discussed.

A review of fifty-six consecutive bronchograms performed with Methocel-Diodrast reveals that this medium has been satisfactory in 66.7 per cent of the cases in which it was used and unsatisfactory in 33.3 per cent of the cases. These results have compared favorably with the information gained from correspondence among others in this country who have been interested in the use of the water-soluble compounds. We have also compared these results with 528 bronchograms performed with Lipiodol and find that in general iodized oils will give satisfactory bronchograms more consistently. Of these 528 cases, only 15.9 per cent were considered unsatisfactory.

Two deaths are reported which followed bronchographies in which Methocel-Diodrast and Methocel-Urokon were used. It is our opinion that the high molecular carbohydrate base precipitated the fatal anaphylactic reactions.

The inherent difficulties with the water-soluble media seem to be factors which are related to technical, toxic, and latent pulmonary changes associated with the use of these drugs.

The currently available water-soluble compounds for bronchography, when used intelligently, are a valuable adjunct to the diagnosis of pulmonary disease. They cannot, however, be considered the ideal agent for bronchography.

REFERENCES

1. Morales, O., and Heiwinkle, H.: A Viscous, Water-Soluble Contrast Preparation, Acta radiol. **30**: 257, 1948.
2. Atwell, R. J., and Pedersen, R. L.: A Water-Soluble Contrast Medium for Bronchography, Dis. Chest. **18**: 535, 1950.
3. Flipse, M. E., Hedberg, G. A., and Krueger, V. R.: Water-Soluble Contrast Media for Bronchography, Presented before the Section on Diseases of the Chest at the 101st Annual Session of the AMA, Chicago, June 10, 1952.
4. Personal communications.
5. Vieten, H.: Erfahrungen bei der Bronchographie mit wasserlöslichen Kontrastmitteln, Per-Abrodil M 60%-viscös, Röntgen-Blätter **4**: 80, 1951.
6. Hentel, W., Cohen, M. B., and Brandenstein, L. C.: Evaluation of Ioduron B in Bronchography. I. A Preliminary Study on Animal Tissues, Dis. Chest. **21**: 280, 1952.
7. Ibid.: Evaluation of Ioduron B in Bronchography. II. A Preliminary Study in Man, Dis. Chest. **21**: 286, 1952.
8. Delie, P., and Sourdat, P.: Use of Iodized Water-Soluble Products for Bronchography, Presse méd. **58**: 1156, 1950.
9. Peck, M. E., Neerkin, A. J., and Salzman, E.: Clinical and Experimental Studies in the Use of a Water-Soluble Agent for Bronchography, Surg., Gynec. & Obst. **92**: 685, 1951.
10. Salzman, E., Peck, M. E., and Neerkin, A. J.: Methocel-Diodrast: A Viscous Water-Soluble Contrast Medium for Bronchography, Radiology **58**: 209, 1952.
11. Hueper, W. C.: Macromolecular Substitutes as Pathogenic Agents, Arch. Path. **33**: 267, 1942.
12. Ibid.: Reactions of the Blood and Organs of Dogs after Injections of Solutions of Methylcellulose of Graded Weights, Am. J. Path. **20**: 737, 1944.
13. Hueper, W. C., Martin, G. J., and Thompson, M. R.: Methylcellulose as a Plasma Substitute, Am. J. Surg. **56**: 629, 1942.
14. Personal communication.
15. Ibers, G., Vieten, H., and Willmann, K. H.: Bronchographie bei Tuberculose, Fortschr. a. d. Geb. d. Röntgenstrahlen **74**: 1, 1951.
16. Willmann, K. H.: Die Bronchographie als Hilfsmittel für die Diagnostik und Lokalisation intrapulmonaler Fremdkörper, Röntgen-Blätter **4**: 148, 1951.
17. Keats, T. E.: Roentgenologic Contrast Media, Bull. Am. Soc. Hosp. Pharmacists **8**: 158, 1951.
18. Thomas, S. S., Henry, G. W., and Kaplan, H. S.: Hepatolienography: Past, Present, and Future, Radiology **57**: 669, 1951.
19. Neuhaus, D. R., Christman, A. A., and Lewis, H. B.: Biochemical Studies on Urokon (Sodium 2,4,6-triiodo-3-acetylaminobenzoate), a New Pyelographic Medium, J. Lab. & Clin. Med. **35**: 43, 1950.
20. Nesbit, R. M., and Lapides, J.: Observations on Urokon, a New Excretory Pyelographic Medium, Univ. Michigan M. Bull. **16**: 37, 1950.
21. Ibid.: Preliminary Report on Urokon, A New Excretory Pyelographic Medium, J. Urol. **63**: 1, 1950.
22. Richardson, J. F., and Rose, D. K.: Clinical Evaluation of Urokon in Pyelography, J. Urol **63**: 1, 1950.
23. Vischer, W.: Veränderungen des Lungengewebes nach Bronchographien mit Joduron B, Schweiz. med. Wchnschr. **81**: 54, 1951.
24. Hellström, B., and Holmgren, H.: The Reaction of the Lung on Bronchography with Viscous Umbradil (Umbradil-Viscös B) (Astra), Umbradil (Astra) and Carboxymethylcellulose: An Experimental Investigation on Animals, Acta radiol. **32**: 471, 1949.
25. Amberson, J. B., Jr., and Riggins, H. M.: Lipiodol in Bronchography: Its Disadvantages, Dangers and Uses, Am. J. Roentgenol. **30**: 727, 1933.
26. Ross, I. S.: Pulmonary Epithelium and Proliferative Reactions in the Lungs, Arch. Path. **27**: 478, 1939.
27. Wright, R. D.: Reaction of Pulmonary Tissue to Lipiodol, Am. J. Path. **11**: 497, 1935.

THE CLINICAL SIGNIFICANCE OF CAVERNOLITHIASIS

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REPORTS dealing with pneumoliths or pulmonary calculi are concerned primarily with the broncholith. Concretions of this type are usually produced by intrabronchial perforation of caseous and partially calcified lymph nodes of the bronchopulmonary or tracheobronchial lymphatics. Schmidt and his associates[3] and Head[1] have recently reviewed their experience and that of others with broncholithiasis and have stressed its clinical significance. Another specific type of pneumolith is located within the lumen of pulmonary cavities and may therefore be termed cavernolith. The purpose of this presentation is to call attention to the possible clinical significance of such intracavitary concretions in the course of pulmonary tuberculosis.

From an etiological standpoint, cavernoliths probably have an origin similar to broncholiths, that is, from a partially calcified tuberculous focus.[1, 3] Calcifications of peripheral caseous foci in the lungs are a frequent occurrence and are most likely to occur in childhood or adolescence but may also occur during the course of adult tuberculosis.[2] In the event the caseous material in such a partially calcified focus discharges into the communicating bronchus, the lesion excavates, and the larger fragments of calcium remain as calculi which lie inside of the resulting cavity. Calcification of cellular detritus and other debris within a cavity offers a possible, but not likely alternate etiological origin for cavernoliths.

Although one would expect cavernolithiasis to be encountered frequently at autopsy, the significance of this condition in the course of pulmonary tuberculosis must have escaped attention as evidenced by the lack of clinical reports in the literature dealing with the subject. For this reason the following brief case reports* are submitted in order to illustrate some of the more important features in regard to the clinical course, diagnosis, and therapy in patients with pulmonary tuberculosis complicated by cavernolithiasis.

CASE REPORTS

CASE 1.—L. M., a 37-year-old man, was symptomless at the time that bilateral upper lobe cavities were discovered in May, 1950. Sputum examination was strongly positive for mycobacterium tuberculosis. Serial roentgenograms (Fig. 1, *A* and *B*) revealed the presence of a flaky cavernolith in the right upper lobe cavity. After a period of six months with conservative management, surgical treatment was advised. Curiously enough, the roentgenograms and laminograms made of the chest prior to surgery did not demonstrate the cavernolith and it was presumed that the fragment had been coughed up. Because of this, first stage thoracoplasty with apicolysis was performed on Oct. 6, 1950. The postoperative course was stormy. There was fever, massive hemoptysis with a marked "bronchial spread" to the middle and lower lobes on the right, and scattered dissemination to the left lung (Fig. 2).

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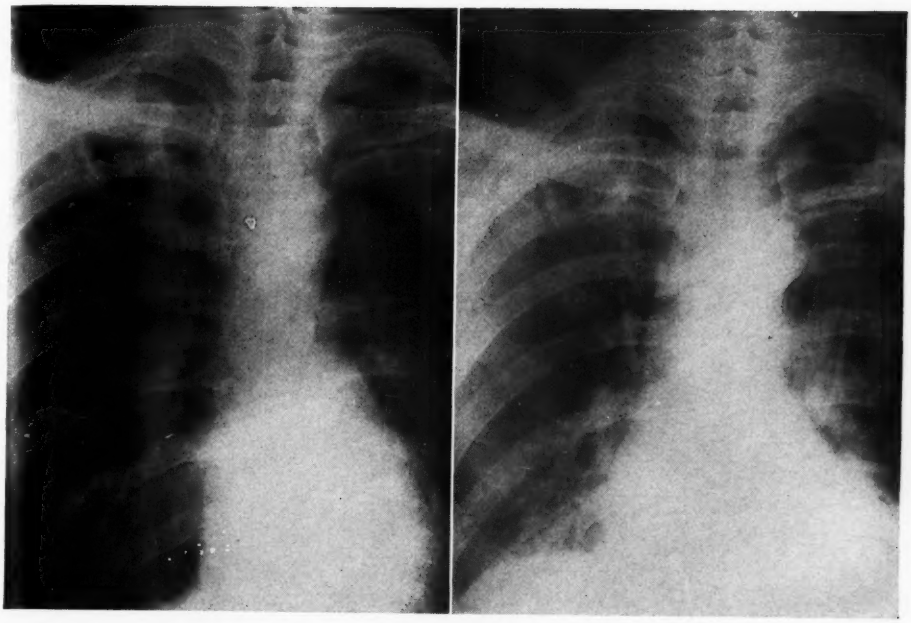


A. *B.*

Fig. 1.—Roentgenograms of the chest (Case 1) demonstrating a cavity with overlying pleural thickening in the right upper lobe. In *A*, the calcified fragment in the cavity is almost horizontal and in *B*, made two months later, the cavernolith is upright.

Fig. 2.—Roentgenograms of the chest (Case 1) made two months after first stage right upper thoracoplasty with apicolysis. There is marked contamination of the lower lobes bilaterally as a result of the severe postoperative hematemesis. The cavernolith had changed position again in comparison to Fig. 1.

Postoperatively, the cavernolith was well demonstrated in the right upper lobe cavity (Fig. 2). The patient recovered from this severe setback after a prolonged course of streptomycin and para-aminosalicylic acid. On Oct. 15, 1951, a right upper lobectomy was performed* and the patient recovered uneventfully. In the resected specimen (Fig. 3) the razor-sharp cavernolith was lying free within an unhealed cavity which measured 2.5 by 2 by 1.5 cm. in diameter.

Fig. 3.—Photograph of sectioned specimen of right upper lobe (Case 1) showing the cavity and the razor-sharp cavernolith which had been repeatedly demonstrated by roentgenography.

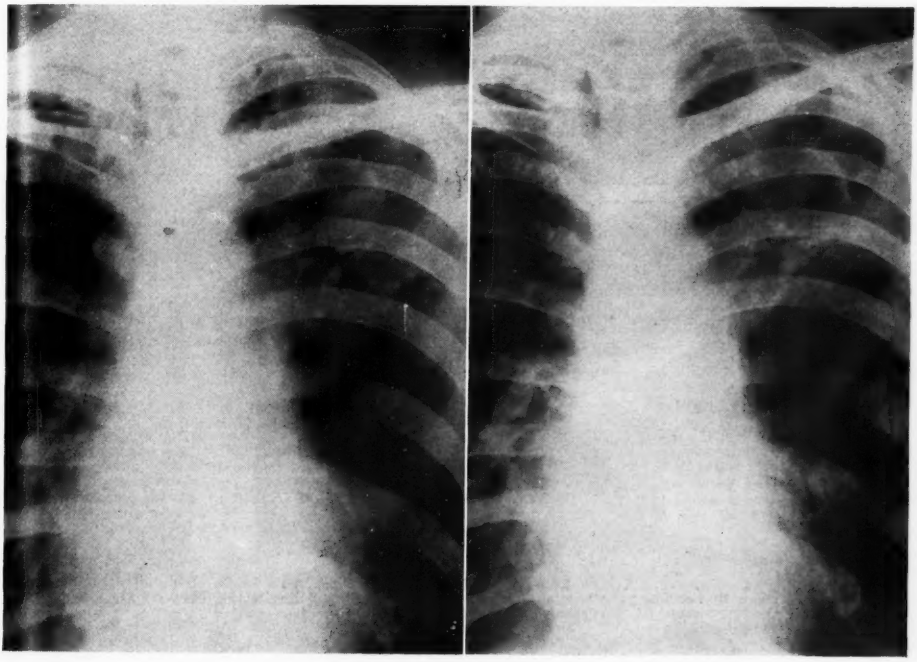
CASE 2.—R. H., a 41-year-old man, was seized suddenly with fever, malaise, and hemoptysis in September, 1945. Roentgenograms revealed cavitation with calcification in the left upper lobe. In the course of the next six months there were repeated similar episodes, and on one occasion he expectorated a tiny fragment of calcified material. During an attack, symptoms could be relieved only by strict and absolute bed rest. Roentgenograms which have since been destroyed indicated that the size and shape of the cavity varied continuously and that the relative position of the cavernoliths changed.

After a long and complicated course, both in and out of the hospital, thoracotomy was performed on July 17, 1946. At this time a left pneumonectomy was done† and the patient recovered uneventfully. The specimen contained multiple cavernoliths, one of which was loosely impacted in a small bronchial opening at the base of the cavity in the left upper lobe.

CASE 3.—R. L., a 34-year-old man, a tutor, was discovered in 1942 to have pulmonary tuberculosis with cavitation in the posterior segment of the left upper lobe. On restricted

*By Mr. Tubbs.
†By Mr. Brock.

activity he did well, but after an episode of strenuous exercise in May, 1949, he became ill again for a short period. During the next twelve months roentgenograms revealed that the left upper lobe cavity periodically filled with secretions and subsequently discharged into the bronchus. The sputum was intermittently positive for mycobacterium tuberculosis. Chest films made in April, 1950 (Fig. 4, *A*), demonstrated the cavity in the left upper lobe which contained a fluid level in the region of the fifth intercostal space posteriorly. A later film in May, 1950 (Fig. 4, *B*), demonstrated the cavity empty of its liquid contents and a small collection of "sand" in the dependent portion of the cavity. Laminogram of the left lung (5 cm. level) (Fig. 5) revealed cavernoliths clearly at a time when the cavity was completely filled with secretion.



A. *B.*

Fig. 4.—*A*, Roentgenogram (Case 3) made in April, 1950, demonstrating a fibrotic process in the left upper lobe with cavitation. In the region of the fifth interspace posteriorly a fluid level is demonstrated in the cavity and collection of calcium is near the base of the cavity.

B, Roentgenogram (Case 3) made in May, 1950, which demonstrates the cavity in the left upper lobe empty of fluid. The calcifications are strongly suspicious of cavernoliths.

On Dec. 4, 1950, a left apical posterior segmental resection was performed* and in ten days was followed by a partial left upper thoracoplasty. Recovery was uneventful. In the resected segment there was a cavity measuring 3.5 cm. in diameter which contained about 20 c.c. of thin pus and multiple granular cavernoliths.

CASE 4.—W. E. M., a 49-year-old man, was found to have pulmonary tuberculosis in 1947, at which time the sputum was positive for mycobacterium tuberculosis, and roentgenograms of the chest revealed extensive cavitary disease of the right lung (Fig. 6). With a combination of sanatorium care and controlled bed rest at home the lesions remained stationary.

*By Mr. Brock.

In February, 1950, the patient became acutely ill with malaise, fever, and leukocytosis and there was fresh pneumonic infiltration in the right lung (Fig. 7). It was noted that the calcifications in the region of the cavity in previous films (Fig. 6) had changed position relative to each other. The pneumonic episode responded to bed rest and to para-aminosalicylic acid which was administered daily. In December, 1950, surgery was being considered but the patient was discharged from the hospital at his own request pending readmission later.

Fig. 5.—Laminogram (Case 3) measured 5 cm. from patient's back, demonstrating the abscess filled with secretions. The appearance of the calcifications in the base of the cavity confirmed the suspicion of cavernolithiasis from films in Fig. 4.

CASE 5.—Mrs. I. G., a 24-year-old housewife, was discovered to have pulmonary tuberculosis by mass radiography in 1943. Gastric washings were positive for acid-fast bacilli and there was scattered infiltration in both upper lung fields on roentgenography. Pneumoperitoneum and temporary left phrenic crush were instituted, and the pneumoperitoneum was maintained for the ensuing five years with partially satisfactory results. Laminograms (Fig. 8, *A* and *B*) of the left upper lobe made in November, 1950, revealed a cavity in the posterior apical segment of the left upper lobe and the cavity contained multiple cavernoliths. At this time the sputum was again positive.

On Dec. 8, 1950, a segmental resection of the left upper lobe was done removing the entire cavity, and the patient recovered uneventfully. The resected specimen contained a tuberculous cavity measuring 3 by 2 by 1.5 cm. in diameter, and there were several small cavernoliths lying free in the cavity.

CASE 6.—M. A., a 22-year-old housewife, was demonstrated to have had pulmonary lesions of tuberculosis at the age of 10 years, after her mother had died of the same disease. After six months of bed rest, she had resumed normal activity until she was 18 years of age, when roentgenograms revealed fresh infiltration in the apices of both lungs. She was admitted to a

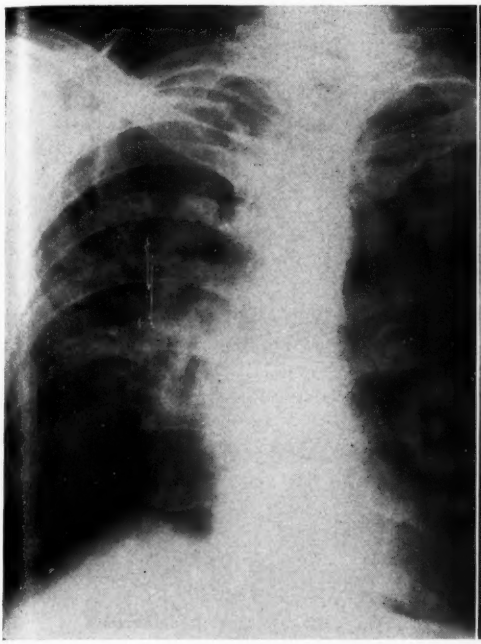


Fig. 6.

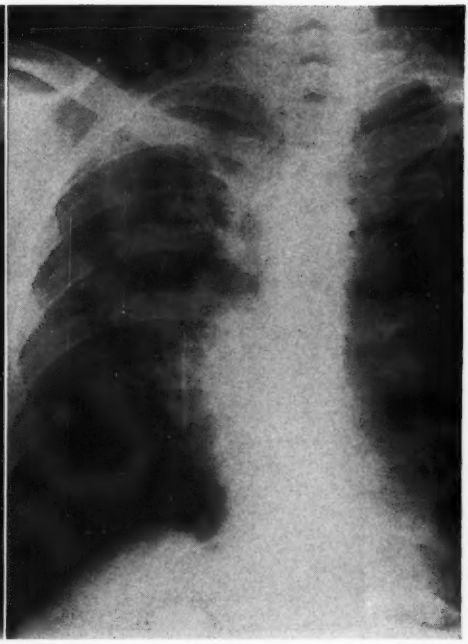


Fig. 7.

Fig. 6.—Roentgenogram of chest (Case 4) demonstrating extensive tuberculous involvement of the right upper and lower lobes with multiple cavitation. In the cavity revealed in the region of the seventh interspace posteriorly several calcifications of varying size are visible.

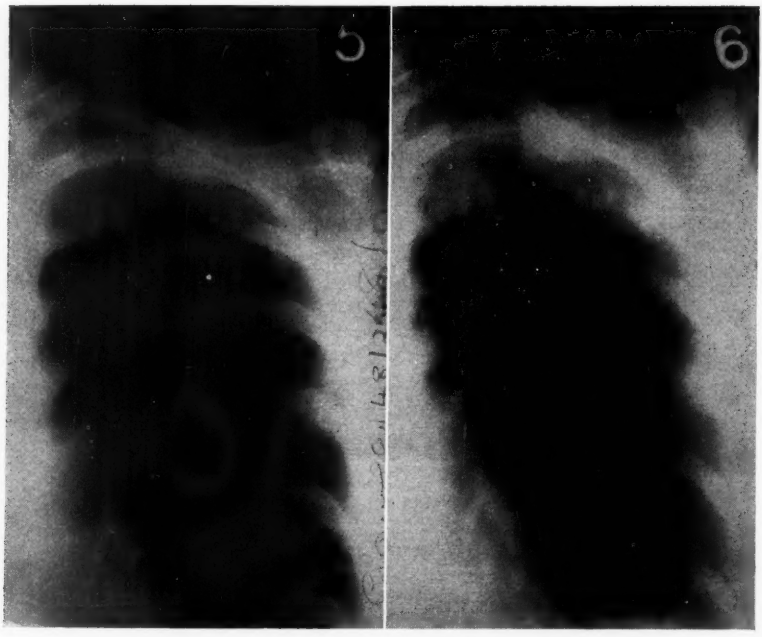
Fig. 7.—Roentgenogram of chest (Case 4) made in February, 1950, after an acute illness. Compared to the findings demonstrated in Fig. 6 in the same patient there is evidence of recent pneumonic involvement on the right. The change in position of the calcium establishes the diagnosis of cavernolithiasis.

sanatorium where gastric washings revealed mycobacterium tuberculosis. During the eighteen months she remained in the sanatorium gastric samples were intermittently positive. At the time of discharge in May, 1950, however, the samples had been negative for three months. Her entire illness was asymptomatic.

She remained bacteriologically negative for the ensuing two years. Early in 1951 she became pregnant, and culture of gastric contents was positive in April, June, and August of that year. She remained on a modified bed rest program and had a normal delivery in October, 1951.

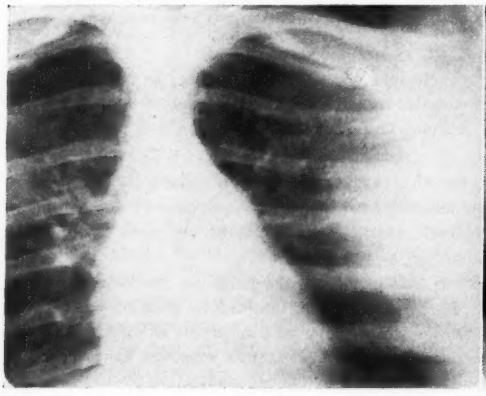
Roentgenograms consistently revealed bilateral infiltrations of the lung, but the lesion in the left apical region was of particular interest. Roentgenograms in the lordotic position made in March, 1951 (Fig. 9), revealed a cavity in the left upper lobe with adjacent calcification. In October, 1951, the cavity had filled with secretions (Fig. 10). It was reasoned that the calcifications which had changed position repeatedly were blocking the communicating bronchus. Review of the films made in the past several years indicated that the sequence of blocking and emptying had occurred repeatedly.

On Dec. 20, 1951, a segmental resection of the left posterior superior segment of the left upper lobe was performed removing the cavity. Recovery was uneventful. When the specimen was incised the cavity, full of thin pus, was encountered (Fig. 11). It contained a half dozen cavernoliths measuring up to 4 mm. in diameter.



A. *B.*

Fig. 8.—*A* and *B*, Laminograms (Case 5) made 5 and 6 cm. respectively from the back, demonstrating an open cavity in the apex of the left upper lobe and at least three cavernoliths of different sizes.



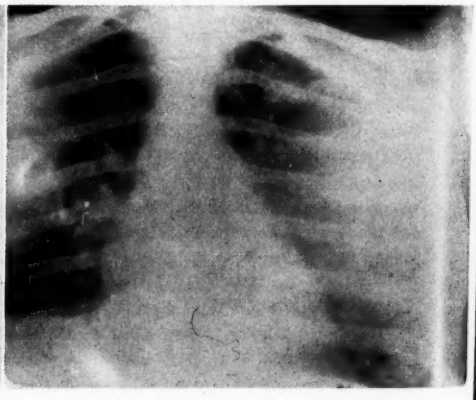


Fig. 9. Fig. 10.

Fig. 9.—Roentgenogram (Case 6) made in March, 1951, in the lordotic position to visualize the apex of the left upper lobe and demonstrating an open cavity in the region of the third intercostal space posteriorly. Calcifications are not well demonstrated in this photograph. Sputum was positive for mycobacterium tuberculosis.

Fig. 10.—Roentgenogram (Case 6) made in October, 1951, demonstrating the abscess cavity previously revealed in Fig. 9, which is now completely filled with secretions. There are multiple calcified bodies visible in the base of the cavity. Sputum and gastric washings contained no acid-fast organisms.

DISCUSSION

Analysis of this small group of patients reveals no symptomatic pattern which is characteristic of cavernolithiasis. Brief comment, however, is due certain clinical aspects of the condition which are demonstrated in these six patients and which may obtain diagnostic significance as experience with cavernolithiasis increases. For the most part the cavernolith is a "silent stone" and produces no symptoms (Cases 3 to 6). It appears, however, that the calculus may pro-

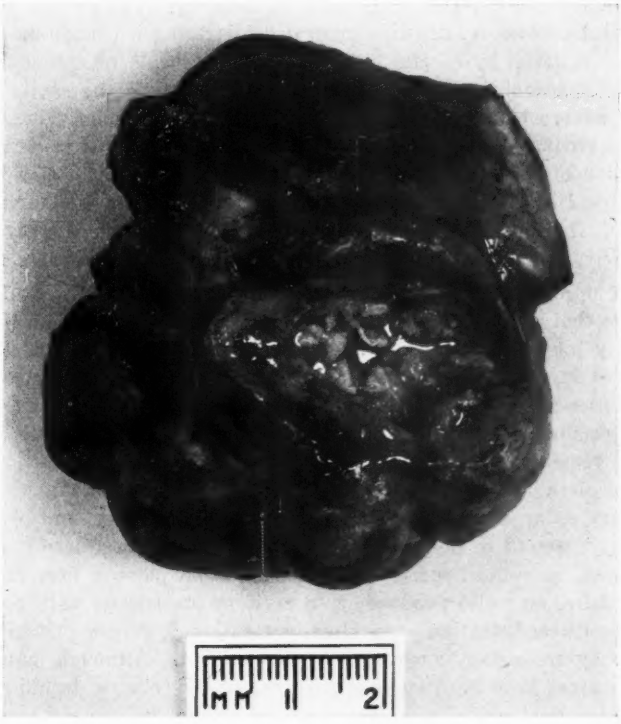


Fig. 11.—Photograph of the sectioned specimen of left upper lobe (Case 6) demonstrating the abscess cavity which contained thin pus. In the lesion are multiple cavernoliths measuring up to 4 mm. in diameter.

duce symptoms either by local trauma and irritation of the pulmonary parenchyma (severe cough, hemoptysis, etc.) or by interference with drainage of the cavity (fever, malaise, pleuritic pain, etc.). Case 2 is a striking example of the marked pneumonic symptoms which may occur as a result of acute obstruction to cavitary drainage. The pneumonic episodes in Case 4 may also have been a manifestation of a blocked cavity. The most marked symptoms suggestive of pulmonary irritation were demonstrated in Case 1. In this instance collapsing the cavity by first stage thoracoplasty probably caused the sharp cavernolith to lacerate a pulmonary vessel producing a massive hemoptysis and dissemination of the disease to previously uninvolved lobes. In contrast to the broncholith,

the cavernolith is rarely coughed up. In Case 2 a small calculus passed through the communicating bronchus, but usually the small caliber of the opening compared to the size of the cavernolith favors impaction of the stone and cavitary obstruction.

Even though the course of the tuberculous process was in some instances altered by the presence of intracavitary calculi, diagnosis usually depends upon roentgenographic findings. Demonstration in a single chest film of calcification in the peripheral lung fields in the neighborhood of a cavity should arouse suspicion that the calcium is lying inside of a cavity. The precise diagnosis of cavernolithiasis, however, depends upon demonstrating a change of position of the calcified material by careful examination of multiple roentgenograms. Ordinarily the cavernoliths occupy a dependent position in the cavity but sometimes may adhere to the walls of the cavity in any position. Therefore, films made in the recumbent positions as well as the erect may assist in demonstrating the migration of the fragment. Other techniques including induced coughing may be helpful in dislodging the calculus and moving it to another position in the cavity. The most valuable technique for demonstrating the cavernolith is laminography. Figs. 5 and 8 are examples of laminography in these cases.

In my opinion therapeutic management of patients with cavernolithiasis differs from that of the usual patient with cavitary tuberculosis and herein lies the necessity for establishing a precise diagnosis. Inert substances lying in infected spaces anywhere in the body interfere with natural healing processes, and in none of these cases of cavernolithiasis did spontaneous healing of a cavity occur. Expectoration of a piece of a calculus occurred in Case 2 but several larger ones remained in the cavity. It may be concluded, therefore, that surgical removal of the lesion is the logical means of obtaining a cure. Techniques of pulmonary collapse including pneumothorax, thoracoplasty, and plombage are theoretically unsound in cavernolithiasis. In the only case where thoracoplasty was employed, near fatal consequences ensued from massive hemoptysis. Collapse procedures may also produce acute cavitary obstruction with possible perforation from overdistention. As already mentioned, severe pneumonic manifestations may accompany such cavitary obstruction. Although many patients in the past must have been successfully treated by collapse techniques, it appears on theoretical and clinical grounds that partial pulmonary resection provides the most rational method of treatment. In five patients so treated the final result was satisfactory.

SUMMARY

Attention is directed to a specific type of pneumolith encountered within pulmonary cavities of tuberculous origin. To these calculi the term cavernolith is applied.

Six patients with cavernolithiasis are reported briefly. In most instances, the stones were silent but occasionally irritative, and obstructive phenomena significantly altered the clinical course.

Diagnosis is rarely made on clinical findings and is usually based upon roentgenography. Careful examination of serial films throughout the clinical

course with particular attention to possible variation in position of intrapulmonary calcification is essential. Laminograms are useful in demonstrating the intracavitary position of such concretions.

Cavernolithiasis is an indication for surgical intervention in pulmonary tuberculosis, and pulmonary resection is recommended in preference to collapse procedures.

REFERENCES

1. Head, J. R., and Moen, C. W.: Late Nontuberculous Complications of Calcified Hilus Lymph Nodes, Am. Rev. Tuberc. **60**: 1, 1949.
2. Rich, A. R.: The Pathogenesis of Tuberculosis, Springfield, Ill., 1944, Charles C Thomas, Publisher.
3. Schmidt, H. W., Claggett, O. T., and McDonald, J. R.: Broncholithiasis, J. THORACIC SURG. **19**: 226, 1950.

INDICATIONS FOR THORACOPLASTY AND PULMONARY RESECTION IN THE SUPINE POSITION

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CHARLOTTE, N. C.

DURING the past two years we have adopted the supine position in certain cases in which pulmonary resection and thoracoplasty were combined as a one-stage procedure. In this position, proper ventilation of the lungs is carried on more automatically and spontaneously; thus the patient is less likely to develop respiratory acidosis. We prefer this position particularly in resections for tuberculosis when pleural symphysis exists, when previous thoracoplasty has been performed, when the patients are acutely ill, and when the vital capacity is low.

If one or more of these conditions exist, the advantages provided by the anterior approach over the commonly employed posterolateral are several. The inclusion of a small anterior thoracoplasty with the pulmonary resection allows a partial collapse of the chest wall which is often highly desirable in resections for tuberculosis. Overexpansion of the remaining lung in such instances may lead to reactivation or spread to the contralateral lung in tuberculosis, and may lead to emphysema after pneumonectomy.

The question may arise as to the ability of an anterior thoracoplasty to produce sufficient thoracic cage collapse and thereby prevent overdistention of the remaining pulmonary alveoli. In our small series of thirty-one resections, the collapse obtained through this procedure appeared adequate to prevent overdistention of the remaining lung.

Any individual who after a two- or three-rib thoracoplasty later requires lobectomy will usually develop atelectasis if a rib is removed in the conventional posterolateral area. In such a situation we have found this procedure particularly indicated. Furthermore, if thoracoplasty has been performed previously the anterior approach is simpler, safer, and preferable. Here, the anterior intact rib stumps and cartilages simplify the problem of finding a cleavage plane; thus a tedious and bloody dissection through a regenerated bony plate posteriorly is averted. Likewise, the normal anatomy of the anterior mediastinum spares the surgeon the difficult problem of creating and establishing a cleavage plane through adherent and dense pleura. The problem is made even simpler since acid-fast lesions are rarely situated anteriorly. Minimal adhesions are produced on a free pleura anteriorly and medially through which the mediastinal structures are rapidly exposed and rapidly identified. In addition, this anterior exposure diminishes the major hazard of excessive blood loss. This is accomplished by controlling and ligating the pulmonary vessels before attempting to extirpate adherent, fibrotic, abscessed lung from the parietal pleura or chest wall.

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Finally, the suggested method of exploration not only technically facilitates the operative procedure, but the patient is maintained in a normal physiologic position throughout surgery. This position reduces to a minimum the hazard of spilling bronchial secretions into the contralateral lung, though it permits excellent pulmonary gas exchange which may avoid dangerous accumulation of carbon dioxide in the blood. The latter problem has been brought to our attention recently by the studies of Beecher and Murphy[1] and also those of Maier.[2] It is thought that the lateral position favors the development of acidosis.

Dehiscence of the bronchus in resection for tuberculosis seemingly is a universal complaint. If a bronchial pleural fistula does develop the situation is not too grim, since already a partial thoracoplasty has been performed. Furthermore, the cavity, which is under tremendous pressure, can be readily decompressed by simply inserting a catheter; or better still, an incision can be made through the soft tissue of the anterior chest wall and the cavity packed with gauze. Hereby, the contamination of the contralateral lung has been eliminated by the gauze occluding the fistula. Then with safety the patient can be turned to the lateral position for completion of the thoracoplasty.

The only disadvantage of the procedure is the greater deformity which follows an anterior thoracoplasty. However, the efficiency and safety of this surgical undertaking, and the preservation of shoulder function must also be of concern to the surgeon. The majority of these patients are in younger age groups in which a long life expectancy is in order. The shoulder muscles are not interrupted or disturbed with this operation. Such an advantage will more than compensate for the deformity of anterior depression which can be readily camouflaged.

OPERATIVE TECHNIQUE

A curved skin incision is made, beginning at the opposite third costal cartilage and extending across the sternum under the mammary gland to the posterior axillary line (Fig. 1). The superior skin flap, with the breast, is dissected free from the pectoralis fascia up to the clavicle (Fig. 2). Unless a long skin incision is used and the flap reflected above the clavicle, the surgeon cannot obtain adequate exposure of the upper ribs and cartilages. The pectoralis major is divided longitudinally about 1 to 2 cm. from the sternum, divided transversely at the fifth costal cartilage, and then retracted laterally (Fig. 3). The second to fifth ribs, inclusively, are removed subperiosteally extending to the posterior axillary line together with their corresponding cartilages (Fig. 4).

Frequently the anterior two-thirds of the first rib is also resected, especially when the inflammatory process has attached the lung tenaciously to the apical pleura. We have experienced no injury to the subclavian vessels in removing the first rib. The pleural space is usually entered through the bed of the third rib, then the mediastinal pleura is exposed and incised. The first vessel encountered in the mediastinum is doubly ligated, transfixed, and severed. The remaining structures are isolated in accordance with the surgeon's choice. Lastly, it is usually the bronchus that is clamped and transected. The lung is then detached from its adherent adjacent structures, largely by sharp and blunt

Fig. 1.

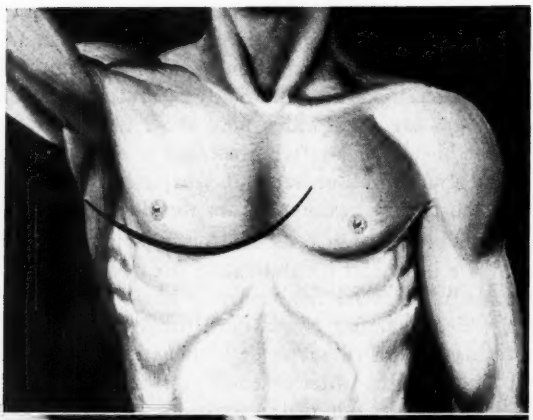

Fig. 2.

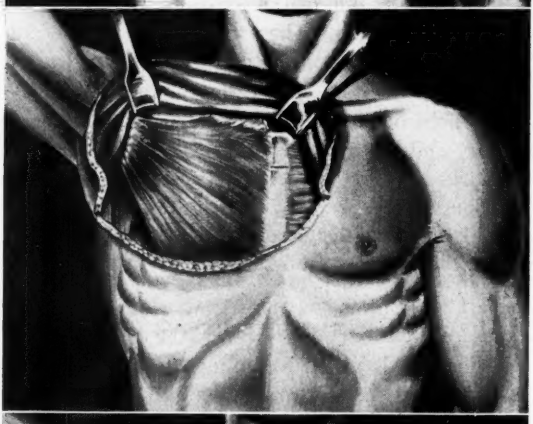

Fig. 3.

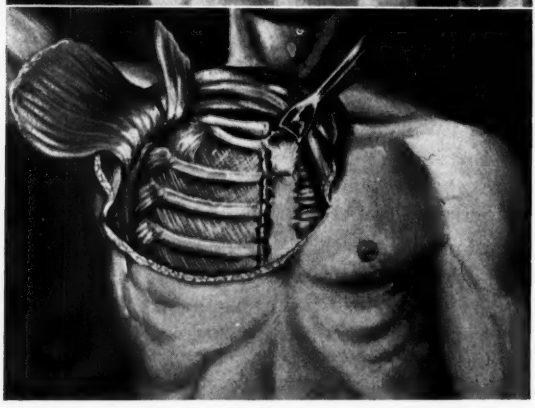

Fig. 1.—A long skin incision beginning at the opposite costal cartilage is extended to the posteroaxillary line.

Fig. 2.—The skin flap is reflected above the clavicle.

Fig. 3.—The pectoralis major muscles are divided and retracted.

dissection which on occasion may require strong arm avulsion. Chest closure is simple since no attempt is made to approximate the pleural or intercostal bundles. It is accomplished by suturing the pectoral muscles, the subcutaneous tissue, and the skin. A frail chest wall has not been a problem. The chest is collapsed stably with abdominal pads held in place by adhesive tape applied longitudinally.

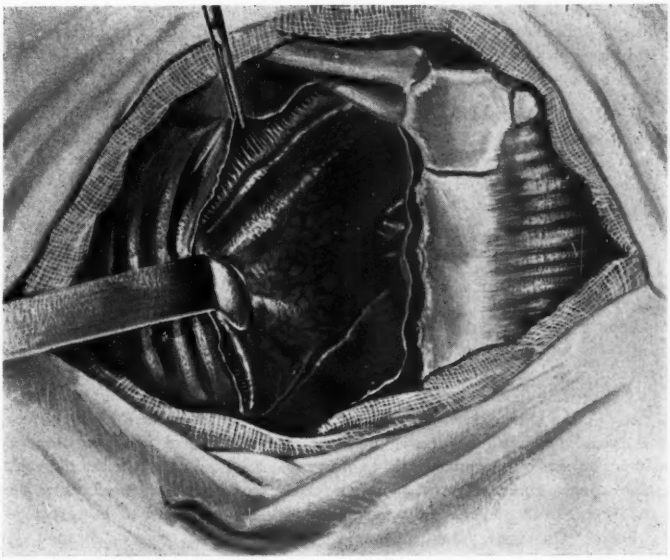

Fig. 4.—The first five cartilages and ribs have been removed as far posteriorly as the posteroaxillary line.

From a technical aspect several points should be emphasized. Following anterior rib resection, the major vessels and mediastinal structures are readily accessible and easily isolated and controlled. In contrast, the patient operated upon in the lateral position has his mediastinal structures "at the bottom of the well." Moreover, if intrapericardial exposure of the vessels becomes necessary, the anterior route lends itself admirably for such an eventuality.

The following case reports of patients, operated upon in the supine position, illustrate a one-stage procedure for thoracoplasty and resection:

CASE REPORTS

CASE 1.—A 28-year-old white man was first admitted to Mecklenburg County Sanatorium eight years ago, complaining of severe headaches, chills, and fever. X-ray examination showed cavity formation, and a diagnosis of tuberculosis was confirmed. He remained one year at the Sanatorium, but was readmitted on three other occasions. Each time he was discharged as apparently arrested. During the third admission a right-sided empyema was drained. Since the left lung had remained stable for eight years, the patient was prepared for pneumonectomy with streptomycin and para-aminosalicylic acid. The bronchus which showed ulceration responded to chemotherapy, and surgery was undertaken.

With the patient in a supine position a curved incision was made which extended from the left third interspace, across the sternum, beneath the right breast to the right posterior axillary line. The right third rib was identified and resected subperiosteally, and then the costal cartilage was removed subperichondrially. The fourth, fifth, and second ribs and cartilages were similarly removed as far as the posterior axillary line. Because of the markedly thickened and adherent pleura, separation of the lung from the lateral and posterior chest wall was impossible. In this circumstance the mediastinum was attacked first. The elements of the hilum were treated by individual ligation technique, and then with considerable difficulty and much bleeding, the lung was bluntly torn from the parietal pleura. Bleeding was controlled with pressure, and the chest wall was closed in layers.

All vital signs remained good, and no complications arose. The patient is now in good health and has been working for eighteen months.

CASE 2.—This 41-year-old white woman had been admitted to the Mecklenburg Sanatorium on four occasions since 1937 because of reactivation of a left pulmonary tuberculosis and empyema. During the last stay (nine months) in spite of streptomycin and PAS, the sputum remained positive. The trachea and mediastinum were deviated to the diseased side. Roentgenographic and bronchoscopic findings limited the pathology to the left lung. A pneumonectomy was performed as described in Case 1. The lung was firmly adherent to the chest wall and diaphragm. Because of the adherence of the lung to the parietal pleura, there was a large amount of bleeding upon avulsing it from its attachments. This bleeding was readily controlled with packs.

Convalescence was without incidence until the fourth month after the operation when she developed signs and symptoms of a bronchial pleural fistula. This complication was managed by inserting a No. 22 catheter into the distended soft tissue in the midclavicular line. The cough was lessened but not controlled until a transverse incision 6 to 8 cm. in length was made through the thin anterior chest wall and the cavity packed with gauze.

A few days later, with the patient placed in the posterolateral position, a seven-rib thoracoplasty was done. The gauze packing prevented any spillage into the opposite bronchus during the operation. The cavity was loosely packed as often as indicated, until three months following the thoracoplasty when only a small fistula remained; but this finally ceased to drain and whistle. One year after pneumonectomy the patient was discharged without any sequelae.

SUMMARY

In certain instances the anterior approach for pulmonary resection is preferable to the posterolateral one because:

1. In the supine position fatal acidosis may be avoided because of better pulmonary ventilation.
2. The incidence of contralateral infection is decreased.
3. It permits a combined thoracoplasty and pulmonary resection in one stage with minimal shock.
4. Cleavage planes in the chest wall and mediastinum are readily obtained in cases where thoracoplasty was previously performed.
5. Mediastinal structures are accessible for ligation prior to the separation of the lung from the chest wall, thus minimizing blood loss.
6. If a bronchial pleural fistula does develop, its consequence is less severe and its correction is more easily accomplished.

REFERENCES

1. Beecher, Henry K., and Murphy, Ann J.: Acidosis During Thoracic Surgery, J. THORACIC SURG. **19**: 50, 1950.
2. Maier, Herbert C.: Blood Stasis in Lungs, Ann. Surg. **130**: 790, 1949.

CARCINOSARCOMA OF THE ESOPHAGUS

Report of a Case With Autopsy Findings

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THE infrequent neoplasms exhibiting more than one cellular component provide interesting material for study and provoke considerable speculation as to their origin. Such a tumor was encountered in the esophagus as an incidental finding in a patient dying of pulmonary tuberculosis.

CASE REPORT

J. K., a Polish man, aged 61 years, was admitted to the Municipal Tuberculosis Sanitarium with a history of having been hospitalized approximately ten years before, in another institution, for pulmonary tuberculosis. He left that institution against medical advice after a four-year stay and worked at odd jobs until the time of his admission here. His family history was negative except for the fact that his mother died at 40 years of age of some "stomach disorder." This man worked at various labor jobs all of his life, did not use tobacco, but was a moderate drinker. Venereal disease was denied. The onset of illness was characterized by a cold with a nonproductive cough, temperature up to 100° F., and a weight loss of thirty pounds. A roentgenogram of the chest and the presence of acid-fast bacilli in the sputum confirmed the diagnosis of pulmonary tuberculosis at a sanitarium dispensary.

Clinical Findings.—Physical examination at the time of admission revealed a tall, fairly well-nourished white man who had several carious teeth and evidence of pyorrhea. The abdomen was slightly protruding but no organs or masses could be palpated. Percussion of the chest revealed some dullness over both upper lung fields, and an occasional râle was heard.

Course.—Approximately two years after admission to the Sanitarium he complained of some difficulty in swallowing. Examination by an otolaryngologist at this time revealed a mass in the right laryngeal ventricle, which, on biopsy, proved to be a papilloma containing some small tubercles. Also, a tumor mass was noted in the mucous membrane overlying the medial surface of the right mandible opposite the first to third molar teeth. This lesion was ulcerated with folded edges, and measured 1.0 by 2.5 cm.; a biopsy proved it to be an epidermoid carcinoma. The laryngeal tumor was excised, the mandibular tumor was treated by x-ray radiation, and the patient's dysphagia gradually disappeared. It is of interest that the painful swallowing the patient complained of was limited to the mouth and throat region. In spite of supportive therapy the patient's pulmonary disease progressed, and he died approximately three years after admission.

Pathology.—At autopsy, examination of the buccal cavity revealed a smooth mucous membrane. No gross abnormality could be seen in the pharynx or larynx. The right lung was firmly adherent to the chest wall over the apical portion by dense fibrous adhesions; the left lung was adherent to the chest wall by less dense adhesions. On sectioning the lungs, a cavity was found in the posterior aspect of the right upper lobe. This cavity measured 6 cm. in greatest dimension and was surrounded by considerable scar tissue. In the opposite lung numerous acinous-nodose lesions were seen, and there was considerable congestion of the uninvolved lung parenchyma. The major bronchi showed considerable congestion. Upon opening the esophagus a firm, pedunculated, smooth, yellow-gray, kidney-shaped tumor which measured 5.0 by 2.5 by 1.5 cm. was exposed (Figs. 1 and 2). This

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neoplasm was attached to the mucosa 9 cm. below the larynx by a thin pedicle. Its surface was in part smooth and in part granular in appearance. On surfaces made by sectioning it was pale gray to yellow-gray in color and resembled a soft fibroma.

Microscopic examination of the esophageal tumor mass revealed that there were two different cellular constituents. The most striking feature was the sarcomatous nature of the stroma which displayed many huge bizarre giant cells and appeared to be actively proliferating (Figs. 3 and 4). In addition, there were nests or groups of epithelial cells which, for the most part, were undifferentiated but which in areas showed some tendency toward rosette formation (Fig. 5). In a preliminary survey of the sections, the impression was given that this might be of neurogenous origin because of the presence of some cells which had the appearance of atypical ganglion cells, and small groups of cells not unlike neuroblasts or sympathicoblasts; however, the consensus of opinion of several consultants[1] was that this represented a carcinosarcoma rather than a tumor of neurogenous origin. Several typical epithelioid tubercles were noted near the periphery of the tumor.

Microscopic studies of the buccal mucosa revealed only moderate fibrosis attributable to the x-ray therapy which had been given approximately seven months previously.

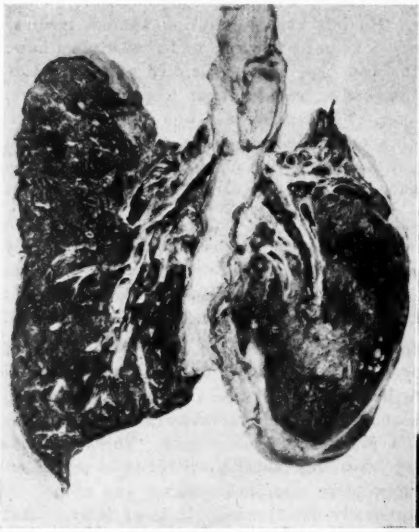

Fig. 1.

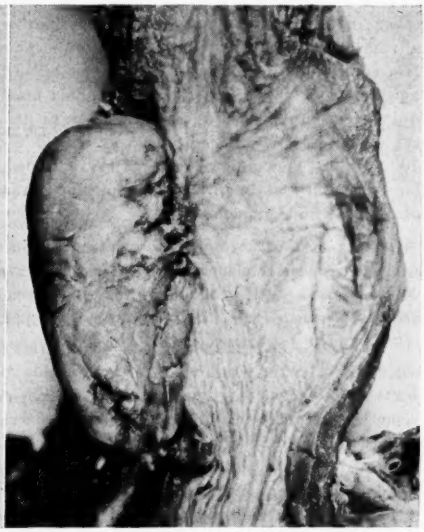

Fig. 2.

Fig. 1.—A photograph of the midsection of the lungs with the esophagus still attached showing a tumor mass 5 by 2.5 by 1.5 cm. located in the upper half of the esophagus at a point 9 cm. below the larynx.

Fig. 2.—Close-up of the tumor mass, demonstrating the pedicle, smooth glistening surface, and lack of mucosal involvement.

DISCUSSION

As early as 1904, Hansemann expressed the opinion that the term carcinoma sarcomatoides should be reserved for the description of a carcinoma with a sarcomatous stroma. He supposedly observed one such case in the esophagus but no histopathologic description was recorded.

Herxheimer, in 1908, characterized carcinoma sarcomatoides as being composed of two distinct cellular types—flat epithelial masses within or surrounded by a sarcomatous stroma.

Fig. 3. Fig. 4.

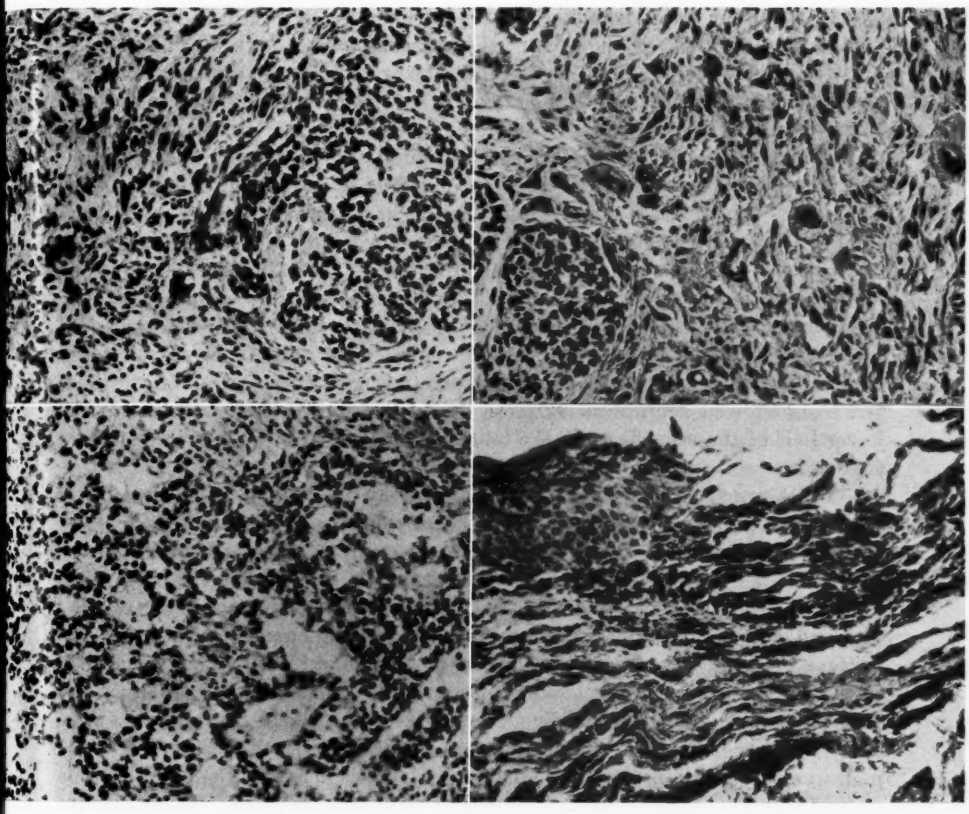

Fig. 5. Fig. 6.

Fig. 3.—Photomicrograph of the tumor mass showing groups of undifferentiated epithelial cells surrounded by a sarcomatous stroma. The stroma shows many bizarre giant cell forms. (Hematoxylin and eosin stain, ×150.)

Fig. 4.—Photomicrograph of a different area showing a similar histologic picture. (Hematoxylin and eosin stain, ×150.)

Fig. 5.—Photomicrograph of an area demonstrating pseudo-rosettes. (Hematoxylin and eosin stain, ×150.)

Fig. 6.—Photomicrograph of the esophageal mucosa at the base of the pedicle demonstrating some activity in the mucosa and an intact basement membrane. (Hematoxylin and eosin stain, ×150.)

In an excellent review Saphir and Bass[2] pointed out that the carcinosarcomatous nature of 153 so-called carcinosarcomas was very questionable. Careful re-examination of sections from tumors thought to be carcinosarcomas revealed that the majority of the neoplasms were probably primary carcinomas. In evaluating the sarcomatous features of the reported carcinosarcomas these authors pointed out that complicating factors may be present which play a role in the alteration of the fundamental histologic appearance of the tumors. These factors are: the spindle-shaped variation of carcinoma cells which may be interpreted as sarcomatous instead of the variant they

actually are; marked anaplasia of the carcinoma cells; chronic inflammation which may alter the morphology of the tumor cells by producing much connective tissue which may be construed as sarcomatous in nature or by provoking a lymphocytic reaction sometimes interpreted as a lymphosarcomatous component of some of these tumors; and the invasion of a benign connective tissue tumor by a carcinoma. Two years later, Pearlman[3] reviewed the cases of carcinosarcoma of the esophagus and examined in detail eight cases of malignancy of the esophagus in which autopsy had been done at Michael Reese Hospital.* These cases were studied with the question in mind as to how their histopathologic picture might be reconciled with the diagnosis of carcinosarcoma, and he concluded that the existence of so-called carcinosarcomas in the esophagus was questionable. Likewise, in 1949, Stout, Humphreys, and Rottenberg[4] reviewed the literature for carcinosarcomas of the esophagus and listed twenty cases in all. Of these twenty cases, only ten were polypoid growths exhibiting epithelial and sarcomatous elements and three of these ten cases showed definite metastases. In nine instances the lesion was in the lower half of the esophagus, in the tenth it was located in the hypopharyngeal region.

There are several interesting aspects worthy of mention in the case being presented. First, no evidence of metastases could be demonstrated, there being no invasion of the esophageal mucosa, even though some activity was noted in the epithelial layer at the site of pedicle attachment (Fig. 6). Second, this individual had two primary tumors—carcinosarcoma of the esophagus and an epidermoid carcinoma of the buccal mucosa. The multicentric origin of tumors is well known, and certainly from a histologic and anatomic standpoint there is no connection between these two neoplasms. Third, this growth was an incidental finding at autopsy, there being no clinical symptomatology or x-ray evidence of the neoplasm prior to death. Inasmuch as the man was extremely ill from pulmonary tuberculosis it is very possible that this masked any symptoms of the lesion, as is so often the case. Last, another feature of this case, not illustrated, was the presence of several early tubercles about the periphery of the tumor mass. Normal esophageal mucosa is rarely, if ever, involved in a tuberculous inflammatory process.

SUMMARY

A case of carcinosarcoma of the esophagus is reported. The pedunculated nature and location of the tumor are illustrated as well as the dual histologic pattern. This was an incidental finding in a case of pulmonary tuberculosis and epidermoid carcinoma of the buccal mucosa.

REFERENCES

1. Armed Forces Institute of Pathology, Washington, D. C., personal communication.
2. Saphir, O., and Bass, A.: Carcinosarcoma, Am. J. Cancer **33**: 331-361, 1938.
3. Pearlman, S. J.: So-called Carcino-sarcoma of Esophagus, Ann. Otol., Rhin., & Laryng. **49**: 805-820, 1940.
4. Stout, A. P., Humphreys, G. H., II, and Rottenberg, L. A.: Carcinosarcoma of the Esophagus, Am. J. Roentgenol. **61**: 461-469, 1949.

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LYMPHATIC DRAINAGE FOLLOWING INTRABRONCHIAL INSTILLATION OF SILVER-COATED RADIOACTIVE GOLD COLLOIDS IN THERAPEUTIC QUANTITIES

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INTRODUCTION

THE use of radioactive metallic colloids promises at the present time to become a useful adjunct to surgery in the treatment of bronchiogenic tumor in man. Recent reports concerning lung cancer in a relatively large series of patients are in surprising agreement in three important particulars,[1, 2, 12, 13] namely: (1) bronchiogenic or primary carcinoma of the lung is diagnosed approximately five to six times more commonly than a generation ago; (2) in only about one-fourth to one-third of the patients are the tumors resectable when first seen; (3) the over-all "five-year cure rate" is in the neighborhood of 5 to 7 per cent. At least two of these groups, Oschner and DeBakey, and Evarts Graham in St. Louis contend that this tumor is now more common in males than carcinoma of the stomach which previously occupied first place. The importance of these statistics cannot be overemphasized and should have quite an impact on the medical profession.

Subject to early diagnosis the treatment of choice in this condition is apparently pneumonectomy, although a few surgeons prefer lobectomy. However, this procedure is applicable only in approximately one-fourth of all the patients who present themselves for study and diagnosis. Metastases by way of the lymphatics is the usual course taken. Deep x-ray treatment may increase slightly the time of survival but by many is considered to be of relatively little value except as a palliative agent. It is not necessary to go into the difficulties involved in the irradiation of deep-seated thoracic lymph nodes, whose position can only be guessed at in any individual and whose irradiation must necessarily involve undesirable side reactions of the pleura and lung parenchyma. Therefore it would seem that any potentially useful procedure which might be used in conjunction with pneumonectomy to cut down the propagation of this tumor process should be a very acceptable one, at least from an experimental viewpoint.

In previous reports we have shown that when radioactive gold colloids are administered intratracheally[10] or intrabronchially[9, 10] a considerable amount of radiation of the lung parenchyma may be achieved. Under these conditions drainage by the thoracic lymphatics is relatively slow and therefore the amount of irradiation to the site of common metastases is limited. Later it was demonstrated that radioactive metallic silver colloids were drained much more rapidly

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by the lymphatics.[6] Their use on a therapeutic scale, however, is obviated at the present time by difficulties in technical production. Ag^{110} colloids, although useful experimentally, are not suitable for therapeutic use due to the long life of this material (225 days half life) which would probably render them carcinogenic in themselves. Ag^{111} is produced by a transmutation reaction $Pd^{110} + n \longrightarrow Pd^{111} + y$, the latter by beta decay being converted to Ag^{111} with a half life of 7.5 days. However the cross section of the Pd to thermal neutrons is relatively low and the abundance of the parent Pd^{110} is only 13 per cent. As a result units obtained from the Oak Ridge pile yield only about 5 mc. of the radioactive silver isotope and these would probably not be sufficient for therapeutic trial. It is planned that in the near future instead of 1 Gm. of Pd being irradiated that the metal in quantities of perhaps 5 Gm. be subjected to thermal neutrons in a higher flux pile. This should make possible activities of about twenty times those now obtainable.

In the meantime we have shown that if radioactive gold colloids are used as nuclei, the dispersion of silver results in a silver-coated colloid which behaves in the same manner physiologically as the silver metal colloids when introduced by bronchoscope. Using such coated colloids in tracer quantities it was found that appreciable amounts were drained by the thoracic lymphatics within from two to five days following administration.[4]

According to the present methods used, there appears to be a minimal amount of silver required to coat such gold nuclei and therefore total radioactivities due to the gold are limited somewhat due to the possible toxic effects of large amounts of silver. In order to obviate this in attempts to use therapeutic quantities of the radioactive gold, bombardments of Au^{197} at the Brookhaven National Laboratories were carried out with resultant specific activities of approximately five times those obtainable previously in the Oak Ridge pile. Following the usual processing* these materials were coated as will be described and administered by bronchoscope using an 18 gauge inner metal tube, the proximal end of which was fitted for a syringe† for injection into the desired lobe of the lung.

The earlier work with the straight gold colloids introduced by this route, in a fairly large series of dogs, indicated that the tolerance dosage was approximately 0.5 to 0.7 mc. per kilogram of body weight, higher dosages usually resulting in death of the animal apparently due to pulmonary inflammatory processes and their sequellae.[9] In contrast, dogs to which the silver-coated colloids have been administered in quantities as high as ten times the amounts just stated have failed to show any untoward clinical manifestations. Although at autopsy some of the latter animals showed considerable degrees of irreversible pathologic changes in the lung lobe involved, nevertheless they, for periods of from one week to several months, exhibited no untoward symptomatology. It is felt that in all likelihood the silver coating, in promoting relatively rapid transfer from the lung parenchyma to the lymphatic system, thus protects the lung from an inordinate amount of irradiation over a relatively prolonged period of time.

*This was done by Abbott Laboratories, North Chicago, Ill.
†Manufactured by Eisle Corporation, Nashville, Tenn.

It seems quite likely that this effect is achieved by reason of an irritation phenomenon, occasioned by the presence of silver which is gradually leached off the colloid, giving rise to enhanced lymphatic drainage. Grossly the pathologic changes in the lung were much less than produced by the gold colloids. Histopathologically it was found in many instances that the lymph node architecture was completely abolished, complete hyalinization having occurred, and in other nodes considerable alteration of the structure having taken place.

Within the past year there has been reported by Muller and Rossier[11] another procedure for irradiation of the lung parenchyma. These investigators employed the microembolic phenomenon obtainable by the introduction of large gold particles introduced intravenously through cardiac catheterization. In an elaboration of their technique they adsorbed soluble gold onto relatively uniform particles of carbon of approximately 30 to 50 micra in size, following which the gold was reduced to the metallic form and subjected to irradiation by thermal neutrons. This latter procedure minimized the amount of small particulate matter which would be carried through the capillary bed and on to the reticuloendothelial system. It is to be stressed that these particles are of about one thousand times the size of those used in the investigations reported by ourselves. The previously mentioned authors show radioautographic evidence of uniform distribution of the radioactive material throughout the lung. Unfortunately we do not have any similar type of evidence for such distribution in our animal work described in this presentation. However, there is every reason to believe that whether the microembolic procedure or the intrabronchial insufflation method is used that the lung parenchyma will be adequately irradiated, in the first case from the capillary bed and in the latter case from the alveoli. It must be kept in mind, however, that most bronchiogenic tumors derive their blood supply from the bronchial artery, and therefore one gains very little in attempting to irradiate the tumor mass proper or the lung parenchyma by either of these procedures. It is especially to be noted that introduction of the large particle gold by the blood vessel route does not result in drainage by the lymph nodes of the thoracic cavity which would seem to be the most important contribution to the use of radiation as an adjunct in surgery as provided by radioactive isotopes.

METHODS

A typical shipment obtained from a Brookhaven bombardment through Abbott Laboratories, as received, consisted of 6.5 ml. of gold colloid containing 0.6 mg. of metallic gold per milliliter and a radioactivity amounting to 50 mc. per milliliter. Left in its original shipping vial, 2 ml. of silver nitrate solution containing 25 mg. of silver was injected through the rubber stopper following which 100 mg. of ascorbic acid dissolved in 2 ml. of pyrogen-free sterile distilled water was added. Actually there is some dispersion of the silver following the addition of the silver itself due to an excess of ascorbic acid which is present in the original gold colloid preparation. The addition of the extra and excess quantity of ascorbic acid results in the production of a deep brown colloid which on high dilution is brown in color to reflected light and a yellowish gray

to transmitted light. Occasionally it was found that the development of color required that the preparation be allowed to stand for as much as an hour. The vial was then reautoclaved and taking into consideration the volume dilution the radioactivity per milliliter was recalculated and the material used for treatment.

Animals were dewormed, vaccinated against distemper, and maintained in the laboratory for a number of weeks prior to use in order that their physical condition would be good. They were anesthesized with pentobarbital sodium (35 mg. per kilogram) and strapped to a table whose upper end was raised somewhat to facilitate drainage downward into the lung. A small-sized bronchoscope was inserted, usually into the right lower middle lobe. An 18 gauge inner metal tube which had been fitted for a syringe was then inserted. A lock-type syringe was attached and the colloid was injected as rapidly as moderate pressure on the plunger would allow. Carried out in open air this results in a stream of colloid emerging about 3 to 4 inches beyond the end of the inner tube and is therefore thought to result in the administration of the material under turbulent conditions which may facilitate the uniform distribution of the colloid in the alveoli of the insufflated lobe. The animal was laid on the floor on his right side until recovery from the anesthesia occurred. In no instance was there any evidence of coughing noted. In these animals the volume of material insufflated was maintained at 5 ml. As stated previously in earlier experiments[4, 9, 10] the colloid was administered at a level of 0.5 ml. per kilogram, but it is not felt at the present time that the optimal volume dosage has been ascertained.

In several of the experiments attempts were made to trace the relative mobility of the radioactive silver (Ag^{110}) coated gold nucleus (Au^{198}) colloid, while in others the material insufflated consisted in an ordinary silver coat on the highly specific radioactive gold nucleus where histologic evidence of damage to the lymph nodes was of special interest. Where the coating and nucleus were both radioactive, samples were counted with a standard commercial beta counter at intervals of approximately one week, weighed fresh tissues being used and stored under refrigeration between counting. In this way radioactivities were measured throughout the dissipation of the radioactivity of the Au^{198} allowing for final determination of Ag^{110} activities and determination by difference of the Au^{198} activities by subtraction of the final from the original measurements. The half lives of these two isotopes being 225 and 2.7 days, respectively, this was relatively simple.

The animals were usually sacrificed by the intravenous administration of an excess of nembutal. All discernible lymph nodes in the thorax were removed for study. Perinodular fat was dissected away and the nodes weighed to the nearest 5 mg. Radioactivity was determined by direct counting using a thin mica-end window counter. Where activities were very high a copper absorber was interposed. The nodes were then placed in 10 per cent formalin for subsequent sectioning and histologic study.

EXPERIMENTAL OBSERVATIONS

Prior to the use of therapeutic quantities of colloids some preliminary studies were carried out in a few dogs in an attempt to follow the courses taken,

respectively, by the silver coatings and the gold nuclei by making use of doubly tagged colloids in which Ag^{110} was employed as the coat for Au^{198} nuclei. A group of four dogs ranging in weight from seventeen to twenty-one pounds were administered Ag^{110} coated Au^{198} colloids in quantities representing approximately 4 mc. of the gold nucleus and only tracer quantities in the silver coat. These animals were sacrificed at five, eight, and twelve days and six months, respectively. Radioactivity measurements in the first three (51-93, 51-94, and 51-96) indicated that the $\frac{\text{gold}}{\text{silver}}$ isotope ratios were such as to show that some of the silver was gradually lost from the lung during the first twelve days and tended to accumulate in the liver. It is of some interest to note that the animal 51-100, sacrificed at six months, still showed considerable activities in a number of the lymph nodes as well as the lungs, especially the treated lobe, in contrast to some animals to be described later which received what is now looked upon as therapeutic quantities of coated colloids. Unlike the gold which is practically insoluble in body fluids, the silver is slowly dissolved and in such form is thought to be highly inflammatory in nature. It is felt that this perhaps constitutes the chief reason why drainage by the lymphatics is facilitated.

The next three dogs 51-71, 51-72, and 51-73 were litter mate female hound mongrels of approximately 7 months of age and weighing sixteen to twenty pounds. They were nembutalized, the bronchoscope inserted, and Ag^{110} coated Au^{198} colloids introduced into a single lobe of the lung. The activity of the silver coat was of tracer orders of magnitude but the activity of the gold nucleus in each case was 50 mc. Earlier studies[9] indicated that the tolerance of the dog to straight gold colloids administered by this route was approximately ½ mc. per kilogram of body weight. Higher doses resulted in death, usually due to pulmonary causes, within ten days to two weeks. These three animals were followed for about a period of six weeks during which time they were in excellent clinical condition and manifested no reaction to the radioactive materials. They were sacrificed by the administration of intravenous chloroform. At autopsy 51-71 showed no necrotic area in the right lung which would correspond to the site of insufflation. There were two grayish white streaks of approximately 5 to 6 cm. in length and about ½ cm. in width on the right lower lobe which it was felt probably represented the site originally involved. Activity measurements (Table I) showed highly divergent quantities of residual radio $silver^{110}$, there being no measurable amounts of Au^{198} activity left after about sixteen half lives of this isotope. It was interesting to note that there was 50 per cent higher concentration of radioactivity in the left mediastinal as opposed to the right mediastinal node. Similarly, the right bronchial node showed practically no radioactivity whereas nearly 300 times the concentration of this activity was found in one of the left bronchial nodes. However, in another left bronchial node there again was very little activity. Unlike many of the earlier animals given silver-coated colloids there was relatively little activity in the node at the bifurcation of the trachea. The lungs showed very little residual activities, one section, through the streaked area of the right lower lobe, however, showing a significantly higher count and indicating only that this was the site of deposition of the colloid. However, one might say that essentially

TABLE I. 51-71. INTRABRONCHIAL Ag^{110} COATED Au^{198} (50 MC.) COLLOID

	WEIGHT OF WHOLE NODE IN GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GLAND
L. mediastinal	.09	137,000	12,319
R. mediastinal	.22	99,000	21,800
L. bronchial A	.19	395	75
L. bronchial B	.05	113,000	5,601
R. bronchial	.11	625	69
R. tracheal	.04	143,000	5,025
Bifurcation	.13	6,900	900
	WEIGHT OF TISSUE SAMPLE IN GM.	COUNTS PER MIN. PER GM.	
L. upper lung	.28	189	
L. mid-lung	.37	111	
L. lower lung	.44	20	
R. upper lung	.36	120	
R. lower A (1)	.35	31	
R. lower B (2)	.63	386	
Liver	.38	540	
Sacrificed after 37 days			

complete drainage had occurred. The liver showed a moderate amount of activity indicating drainage of silver by that organ.

The previous animal's litter mate, 51-72, showed quite a different picture than her sibling. The levels of radioactivity remaining are considerably higher than those in the previous dog. At autopsy the right lower lobe showed a grossly necrotic area of approximately 2½ cm. in diameter which largely resembled such areas found in the lung following the intrabronchial introduction of the gold colloid alone. The right lower lobe, that part which appeared more normal, contained over four times the concentration of radioactivity as the necrotic area in the right lower lobe (Table II). This may merely mean that the silver sloughed out following the dissipation of the irradiation due to the gold. In this animal the right mediastinal nodes, of which there were two, showed decidedly higher concentrations than the left. However, the left bronchial node had approximately twice the activity of the right bronchial node. Also there were two right tracheal nodes which showed a wide discrepancy in their concentration of radio silver and the left tracheal node contained a concentration equal to one of the right tracheals and four times the concentration of the other right tracheal node. The right axillary node taken as a control showed background activity as might be expected.

The third litter mate of this group, 51-73, like 51-71, showed no gross lesion of the right lower lobe into which the colloid had presumably been insufflated. All lung blocks had exceedingly low activities (Table III). The left and particularly right mediastinal node showed high levels of silver activity and the right tracheal node showed moderately high levels. Other nodes were quite low in their silver content. All nodes and lung tissues from this animal were counted on four occasions and the activities were essentially the same in all instances indicating that the latter were derived from the Ag^{110} and none from any residual gold activities.

TABLE II. 51-72. INTRABRONCHIAL Ag^{110} COATED Au^{198} (50 MC.) COLLOID

	WEIGHT OF NODE IN GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GLAND
L. mediastinal	0.035	90,000	3,146
R. mediastinal A	0.03	250,000	7,608
R. mediastinal B	0.025	360,000	9,064
L. bronchial	0.30	3,400	1,028
R. bronchial	0.14	1,940	272
L. tracheal	0.07	23,500	1,648
R. tracheal A	0.14	6,300	887
R. tracheal B	0.05	21,700	1,089
Bifurcation A	0.15	22,600	3,384
Bifurcation B	0.15	11,000	1,655
R. axillary	0.075	133	10
	WEIGHT OF TISSUE SAMPLE IN GM.	COUNTS PER MIN. PER GM.	
L. upper lung	0.21	53	
L. lower lung	0.58	15	
R. upper lung	0.53	430	
R. middle lung	0.27	1,380	
R. lower lung	0.68	14,500	
R. lower necrotic	0.64	2,900	
Liver	0.72	110	
	Sacrificed after 42 days		

Dog 52-183 was a mongrel about 2½ years old, weighing forty-five pounds, to whom was administered 120 mc. of a silver-coated gold colloid intrabronchially. After six days, during which period he appeared to be in excellent clinical condition, the animal was sacrificed with nembutal. The lungs on both the right and left sides were edematous and when cut exuded a free-running serous fluid. Otherwise there was nothing grossly of interest.

The radioactivity data are shown in Table IV where it is indicated that there was some spilling over of the colloid from one lobe of the right lung to

TABLE III. 51-73. INTRABRONCHIAL Ag^{110} COATED Au^{198} (50 MC.) COLLOID

DATE COUNTED	3/15/52	3/17/52	3/19/52	3/25/52	
WEIGHT OF NODE IN GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GLAND
L. mediastinal	0.05	66,000	70,000	67,000	63,000	3,300
R. mediastinal	0.07	174,000	167,000	197,000	180,000	12,200
L. bronchial	0.30	47	20	13	30	14
R. bronchial	0.17	106	47	41	47	18
L. tracheal	0.05	4,000	3,800	3,700	3,600	200
R. tracheal	0.03	21,200	18,800	19,000	18,000	639
Bifurcation A	0.22	41	46	32	18	9
Bifurcation B	0.69	51	26	32	41	35
R. axillary	2.28	4	8	2	4	9
WEIGHT OF TISSUE SAMPLE IN GM.					
L. upper lung	0.67	50	31	24	13	
L. lower lung	0.91	19	11	8	7	
R. upper lung	0.58	33	36	29	22	
R. middle lung	0.70	17	20	7	—	
R. lower lung	0.71	25	35	6	21	
Sacrificed at end of 42 days						

another. Of chief interest, however, is the fact that all of the nodes taken from the thorax showed values of radioactivity concentrations approximating that of the treated lobe or as high as eighteen times as much in the case of the right mediastinal node. As has been pointed out before, there is indication of excellent cross drainage as shown by the activities in the nodes taken from the left side. From a standpoint of time element this animal showed an excellent degree of lymphatic drainage, and adequate irradiation of all the thoracic lymph nodes was accomplished. One may only approximate the roentgen dosage received by the lymph nodes, assuming uniform distribution of the colloid throughout the node.

TABLE IV. 52-183. INTRABRONCHIAL Ag COATED Au^{198} COLLOID (120 MC.)

	WEIGHT OF NODE	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GLAND	PER CENT TREATED LUNG
L. mediastinal	0.09	19,100	1,730	1,310
R. mediastinal	0.11	26,500	2,925	1,830
L. sternal	0.73	4,700	3,430	325
R. sternal	0.81	3,560	2,840	245
L. tracheal	0.13	7,280	947	500
R. tracheal	0.28	15,800	4,440	1,090
L. bronchial	0.36	1,260	452	87
R. bronchial	0.10	1,530	153	107
Bifurcation	0.16	5,050	810	350
L. upper lung		216		15
L. lower lung		64		4
R. upper lung		690		47
R. middle lung		1,450		100
R. lower lung		1,050		72
Liver		49		3.4
Heart		26		1.8

Sacrificed after 6 days

In order to calculate the equivalent roentgen dosage delivered to the various tissues, one is forced to make a number of assumptions. Among these is one, admittedly incorrect, to the effect that radioactive material remains in the same site at which it was found at time of sacrifice. From the various animals studied in this group this is obviously not true but for the purposes of an estimate we may take in animal 52-183 the distribution as found at the end of six days. In this animal we must further assume that the tissues examined contained the total of 120 mc. of gold administered. Taking an average lung lobe as 40 Gm. and the liver of this animal to be 450 Gm., and making the necessary calculations using the K_β for gold of 76, we find that the approximate beta equivalent roentgens delivered[3, 8] are approximately 2,500 e.r. to the liver. This is approximately that used in therapeutic management of chronic leukemias and is well tolerated by this organ.[5, 7] That amount of radiation delivered to the lung tissue will approximate 35,000 e. r. and to the lymph nodes approximately one-quarter of a million roentgens.

Dog 52-186, a male adult mongrel chow about 2 years old, had 50 mc. of a silver-coated gold colloid administered by bronchoscope and the animal was sacrificed ten days later by the administration of intravenous nembutal. The

clinical condition of the animal in the interim was excellent. Although most of the radioactivity was found in the right lower lobe of the lung nevertheless both other lobes of the right lung showed fairly considerable amounts of activity (Table V). In contradistinction to the other animals described receiving therapeutic doses there was rather poor drainage of the colloid by the thoracic lymphatics. Only the lymph node at the bifurcation of the trachea had accumulated any appreciable amount of radioactivity and this was only 66 per cent of the concentration per gram of fresh tissue as that found in the treated lobe of the lung.

TABLE V. 52-186. AG COATED Au^{198} (50 MC.) COLLOID INTRABRONCHIALLY

	WEIGHT OF NODE IN GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER GLAND	PER CENT TREATED LOBE
L. sternal node	.31	96	30	0.6
R. tracheal node	.21	43	9	0.2
L. mediastinal node	.07	415	29	0.6
R. mediastinal node (fat)	.78	520	405	8
L. bronchial node	.47	280	131	3
R. bronchial A node	.34	2,030	692	14
R. bronchial B node	.16	6,460	1,036	21
Bifurcation node	.69	4,680	3,235	66
Axillary node	.55	13	7	0.1
	WEIGHT OF SAMPLE IN GM.			
L. upper lung	.18	326	59	1.2
L. lower lung	.33	140	46	0.9
R. upper lung	.51	1,900	968	20
R. middle lung	.74	2,600	1,932	40
R. lower lung	.96	5,100	4,900	100
Liver	1.1	8	9	0.2
	Sacrificed after 10 days			

Dog 52-173, a male mongrel of about 2 years of age and weighing thirty-three pounds, was given a silver-coated gold colloid representing 85 mc. of Au^{198} into the right lower lung by bronchoscope. At the end of twenty-six days, during which time the clinical condition of the animal appeared to be excellent, he was sacrificed with nembutal. Approximately one liter of fluid was found in the pleural cavity although the lungs grossly appeared to be normal pink in color and there was no sign of hemorrhage. Activity measurements shown in Table VI indicate that drainage from the treated lung by this length of time was nearly complete. Distribution of radioactivity in the various thoracic lymph nodes was quite satisfactory reaching as much as twenty-four times that of the treated lung in the case of the left sternal node. It is again of interest that the left mediastinal, left bronchial, left sternal, and left tracheal nodes all showed higher activities than their corresponding right-sided nodes. Therefore there seemed to be a preferential drainage to the left side in this particular animal.

No attempt is made in this brief presentation to include a complete study of the pathology and histopathologic findings of the tissues and neither is there an attempt made to correlate comprehensively such findings with the radiation delivered. This will be done in more detail at a latter date. However, a number

TABLE VI. 52-173. AG COATED Au^{198} COLLOID INTRABRONCHIALLY (85 MC.)

	WEIGHT OF NODE IN GM.	COUNTS PER MIN. PER GM.	COUNTS PER MIN. PER NODE	PER CENT TREATED LUNG
L. mediastinal	.31	7,900	2,453	1,600
R. mediastinal	.14	8,100	1,131	740
L. bronchial	.24	750	180	118
R. bronchial	.20	835	167	108
L. sternal	.60	6,130	3,680	2,400
R. sternal	.77	4,050	3,117	2,000
L. tracheal	.37	930	343	220
R. tracheal	.80	81	65	43
L. bifurcation	.66	650	429	280
	WEIGHT OF SAMPLE IN GM.			
L. upper lung	.41	37		10
L. lower lung	.50	24		8
R. upper lung	.41	71		19
R. middle lung	.52	40		13
R. lower lung	.50	310		100
Liver	.79	530		270

Sacrificed 26 days following instillation

of selected sections varying widely in their residual radioactivity content were submitted for histopathologic examination and the results are briefly described here. It is to be noted that in general the changes seem to parallel quite closely the degree of residual activity present in the tissues. There are one or two exceptions. It should be pointed out that the columnated figures of radioactivity in Tables I to VI expressed in counts per minute per gram of fresh tissue are relative values, inasmuch as some samples were of such high activity, it was necessary to use adsorbers interposed between the mica window counter and the sample. In other instances the counts were relatively low due to protracted time intervals between insufflation of colloid and sacrifice and it was possible to count directly under the window.

*Histopathology**.—

A. Dog 51-71

1. Left mediastinal lymph node was hyalinized with obliteration of afferent and efferent lymphatic channels and showed early calcific deposits. There were no marginal or medullary sinuses and no lymphatic or reticuloendothelial tissue present.

2. Right mediastinal lymph node was similar to left mediastinal lymph node with glassy hyalinization. There was fat necrosis with sheaths of fatty acid crystals and thrombosis of lymphatics.

3. Right bronchial lymph node showed hyperplastic lymphatic follicle. No radiation effects were evident. Marginal sinuses were difficult to make out.

4. Right tracheal lymph: subtotal (80% ±) hyalinization with some persistence of reticular elements.

5. Bifurcation was similar to right bronchial node.

*We are deeply indebted to Dr. R. L. Holman for his kindness in reviewing some of the histopathologic sections on these animals.

6. Lung: right lower lobe showed patchy fibrosis with a question of lipoidal type pneumonia. There was a questionable thrombosis of one of the blood vessels.

7. Iung: right lower lobe similar to but not as marked as in No. 6.

8. Left lower lobe showed patchy interstitial pneumonia with questionable foci of necrotizing arteritis.

Summary: (1) Lymph nodes can be obliterated by the technique employed. (2) In process of obliteration both lymphatic and reticuloendothelial tissue undergoes coagulative necrosis with subsequent hyalinization and calcific deposits. (3) Both afferent and efferent lymphatic channels appear to be obliterated in the process. (4) Reaction in the lung is not striking and is patchy.

B. Dog 51-72

1. Right mediastinal lymph node (a) showed complete hyalinization with collapsed sinusoids and a question of arteritis. Pigment in this node was felt probably to be anthracotic but the possibility of its representing silver or gold has not been excluded.

2. Right mediastinal lymph node (b) was similar to (a) in No. 1 and with arteritis.

3. Right bronchial lymph node presented a picture of atrophy of lymphatic tissue, reticuloendothelial hyperplasia, early necrosis and hemorrhage (especially about blood vessels). The architecture of the lymph node persisted in focal areas, both cortical and medullary.

4. Bifurcation node (a) was similar to but less marked than right bronchial lymph node No. 3. Some germinal centers were present.

5. Right axillary lymph node was similar to bifurcation No. 4.

6. Lung: left upper lobe showed minimal interstitial reaction with lipophages.

7. Lung: right lower lobe, had pneumonic process especially hemorrhage and slightly more marked than in No. 6.

8. Lung: right lower lobe, had large areas of coagulation necrosis with questionable thrombosis.

Summary: Findings in this dog were similar to those in 51-71 but in addition suggest: (1) The necrosis of the right lower lobe may be related to infarction. (2) Slight to moderate doses of radioactivity exposure lead to atrophy of lymphatic tissue with reticuloendothelial hyperplasia.

C. Dog 51-186

1. Right bronchial lymph node (a) showed early necrosis especially of lymphatic tissue as well as some reticuloendothelial hyperplasia. Marked anthracosis was noted especially in medullary part.

2. Right bronchial lymph node was similar to (a) just described.

3. Right tracheal lymph node had few active germinal centers and showed early reticuloendothelial hyperplasia. There was erythrophagocytosis in medullary sinuses.

4. Bifurcation lymph node was similar to No. 3 with large avid phagocytes engulfing necrotic lymphocytes in remnants of germinal centers.

5. Left sternal lymph node was similar to bifurcation No. 4.
6. Axillary lymph node was similar to No. 4 and No. 5.
7. Liver was not noteworthy.

Summary: In ten days there was stimulation, exhaustion, and phagocytosis in germinal areas, and some reticuloendothelial hyperplasia with hemorrhage in sinusoids. Apparently this represents the early stages in the process that ends in hyalinization.

DISCUSSION

There are several important points which must be considered in light of the purpose of the described experiments. If we hew to the proposed line of attack of bronchiogenic tumor by the instillation of these radioactive colloids intrabronchially prior to pneumonectomy we are presupposing that such colloidal material would behave in the diseased human organism similarly to that which is found to obtain in the normal dog's pulmonary system.

Several points of interest are worthy of mention. The frequency with which the contralateral nodes concentrated radioactivity is eloquent evidence of cross drainage of the lymphatics and fits in with the findings of metastatic processes in breast and lung tumors. However, drainage by the various nodes appears to be quite haphazard. For example, in Dog 51-71 there were two bronchial nodes found on the left side; one of which showed 250 times the concentration of radioactivity as the other. Again in Dog 51-72 two right tracheal nodes differed in concentration of the silver by a factor of 3. In 52-183 the distribution of the coated colloid was excellent regarding the findings in the thoracic lymph nodes. On the other hand in certain other animals there was a disappointing amount of concentration of the colloid in some lymph nodes and inadequate irradiation of such tissue resulted.

We note that in Dog 51-72 the lungs showed, especially in the lobe into which the material was administered, considerably higher radioactivities than in the two dogs, 51-71 and 51-73, the latter having manifested no gross pathologic lesions. The amount of material at hand is too meager to enable us to speculate why in this particular animal the silver was not drained as completely as in the others. In the case of Dog 51-73, repeated measurements were made of the lymph nodes and lung blocks in order to reassure ourselves that the residual activities were due to the Ag^{110} isotope and the data substantiate this (Table III). Again, in this animal the tremendous variations in the radioactivity concentrations in the various nodes are apparent. In several other animals where sacrifice occurred at rather belated intervals the concentration in the lymph nodes was many times that in the insufflated lobe of the lung. Such intervals between instillation and sacrifice sometimes are of a length which is far longer than the time necessary for the dissipation of all the radiation from the gold nucleus. Therefore it may well be that for the most successful irradiation of such nodes, we shall ultimately be well advised to resort to use of the Ag^{111} isotope which, having a half life of seven and one-half days, may be much more suitable for prolonged irradiation in metastatic bronchiogenic tumor.

As to the uniformity of distribution of the colloid in the lymph nodes it might be said that the few autoradiographs which have been made of these tissues suggest a rather spotty distribution. A great deal of further experimentation must be carried out to assess the factors which determine the deposition of colloid in different lymph nodes.

The extremely variable distribution of the radioactive material in tissues demands a large margin of safety, regarding both minimal dosage compatible with a cancericidal effect in the lymphatic system and a dosage which is not too deleterious to other tissues. If, for instance, one considers Dog 52-173 (Table IV) which was sacrificed twenty-six days following intrabronchial instillation of the colloid it would be found that the liver radiation dosage was quite considerable. However, we have in other studies found that this organ is capable of withstanding relatively massive amounts of irradiation before irreversible pathologic changes are undergone.[5, 7] The wide variations in the dosage of radiation delivered to the lymph nodes is partially compensated for by the fact that we are, in most cases, dealing with many times the probable cancericidal dose.

Taking into consideration the fact that the half-path of the gold beta particles is 0.4 mm. in tissue this would allow for the order of magnitude of only forty cell diameters for a lethal effect to be attained regarding malignant cells. On the other hand, in working in the order of 10^5 equivalent beta roentgens, we are in a range where there is probably no inconsiderable amount of effect due to the relatively small gamma component of this isotope and in the final analysis it may well be that a satisfactory therapeutic dose may be realized. Of course, as stated elsewhere, the foregoing values are based on normal dog tissue and it remains to be seen whether such factors as blockage of lymphatic channels by tumor tissue in the cases of human malignancy will operate to render impossible the delivery of adequate amounts of irradiation under such conditions.

Throughout all such conjecture one must keep in mind that all calculations at the present time are carried out on a basis of rather sweeping assumptions due to the transient behavior of the radioactive colloid in the tissues under consideration. It is not likely that dosage calculations shall ever be as simple as those for x-irradiation or for implants of long-lived material (for example, radium) and it is well recognized that the difficulty of calculating irradiation dosage for these latter is complicated enough.

It should be noted in favor of the likelihood of obtaining adequate irradiation despite inhomogeneous distribution of the colloid in the nodes that, for example, in Dog 51-71, several of the nodes which had received the largest amount of radiation had atrophied to the point that they weighed only from 40 to 90 mg. The total dimensions of the nodes at such a time were such that adequate beta irradiation must have been accomplished in spite of the short path of the beta particle of the isotope used. In the illustration of the photomicrograph of such a node (Fig. 1), the entire node is represented. Of course we cannot say for certain how much of the atrophy preceded the partial or complete dissipation of the energy from the contained isotope.

What appears at present to be a limiting factor in the efficacy of the instillation of radioactive colloids intrabronchially as a form of treatment is represented by the widely discrepant activities exhibited by the various lymph nodes studied. Our knowledge of the lymphatic drainage of the thoracic cavity as well as other areas of the body is in a parlous state. Further use of colloids with and without concomitant studies of the effect of localized inflammatory processes may assist in divulging which factors are operating to cause concentration of these materials in certain nodes. The dog is notoriously prone to develop pulmonary infections and it may well be that certain nodes at various times are subject to inflammatory reaction and therefore may concentrate materials to a different extent than near-by nodes.

Fig. 1.—Dog 51-72. Right mediastinal node. (Hematoxylin and eosin; ×150.)

As stated before in dealing with human pathologic conditions the probability of lymphatics being plugged by tumor tissue and, therefore, being impervious to transport of the colloid to the nodes must be considered. Studies are underway in several far-advanced cases of bronchiogenic tumor in human beings to determine the degree of deposition of such colloids under these circumstances. The possibility should be kept in mind that development of collateral lymphatic drainage under such circumstances may possibly come to the aid of the therapist.

SUMMARY

The distribution of silver-coated radioactive colloidal gold particles, following their intrabronchial administration in dogs, has been studied at levels of radioactivity which are estimated to be in a therapeutic range for treatment of metastatic lesions in bronchiogenic tumors.

A short series of experiments in which the silver coat as well as the gold nucleus were radioactive indicates that the silver coat is gradually leached off in the lung and is carried to the liver for ultimate secretion, probably by the biliary tract.

It is found that the silver assists in the transport of the radioactive gold nucleus by way of the lymphatics to the thoracic nodes thus facilitating irradiation of these common sites of metastatic processes.

Estimated roentgen equivalent dosages to various tissues of interest would suggest that the amount of irradiation encountered by the liver is well within tolerable limits by a factor of perhaps 10 times. Dosages to the lung into which the material was introduced are relatively high but this tissue is considered expendable since in most cases pneumonectomy is planned when treatment is anticipated. Dosages to the lymph nodes are estimated to be of the order of several hundred thousands equivalent beta roentgens. It is felt that discrepancies in uniformity of distribution in such tissues would be well taken care of by the large factor of safety over estimated cancericidal doses necessary to deal with metastatic processes. The possibility of obstruction in the cases of metastatic tumor involving lymphatic channels is considered. Also the possibility of collateral lymphatic drainage under such conditions is hypothecated.

Study of drainage by the lymph nodes in cases of bronchiogenic tumor in human beings is obviously necessary before the distribution of radiation can be depended upon as a therapeutic procedure.

REFERENCES

1. Ariel, I. M., Avery, E. E., Kanter, L., Head, J. R., and Langston, H. T.: Cancer **3**: 229, 1950.
2. Graham, E. A.: S. Clin. North America **30**: 1259, 1950.
3. Hahn, P. F.: A Manual for Artificial Radioisotope Therapy, New York, 1951, Academic Press, Inc.
4. Hahn, P. F., and Carothers, E . L.: Brit. J. Cancer **5**: 400, 1951.
5. Hahn, P. F., Jackson, Marvin, and Goldie, Horace: Science **114**: 2960, 1951.
6. Hahn, P. F., Rouser, George, Brummitt, Houston, Moorehead, Joseph, and Carothers, E. L.: J. Lab. & Clin. Med. **39**: 624, 1952.
7. Hahn, P. F., Staggers, F. E., Goldie, Horace, and Jackson, Marvin A.: (In preparation).
8. Marinelli, L. D., Quimby, E. H., and Hine, G. J.: Am. J. Roentgenol. **59**: 260, 1948.
9. Meneely, G. R., Auerbach, S. H., Woodcock, Clarence, and Hahn, P. F.: (In preparation.)
10. Meneely, G. R., Kory, R. C., Auerbach, S. H., and Hahn, P. F.: Federation Proc. **1**: 10, 1951.
11. Muller, J. H., and Rossier, P. H.: Acta radiol. **35**: 449, 1951.
12. Ochsner, A., and DeBakey, M.: Surgery **8**: 992, 1940.
13. Steiner, Paul E.: Cancer Research **12**: 455, 1952.

INTRAPERICARDIAL DISSECTION IN LEFT PNEUMONECTOMY FOR BRONCHIOGENIC CARCINOMA

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PULMONARY resection is generally accepted as the treatment of choice in cases of carcinoma of the lung in which the lesion is operable. There is as yet, however, no general agreement as to what constitutes an adequate radical resection in cases of cancer of the lung. One approach to a more extensive resection of tissue has been the employment of intrapericardial dissection.

Intrapericardial dissection is practicable in the performance of both right and left pneumonectomy. The problem is somewhat different in cases in which a right pneumonectomy is necessary as contrasted with those in which a left pneumonectomy is necessary owing to the anatomic differences pertaining in the two hemithoraces. To avoid confusion regarding this, we shall limit this presentation to a discussion of certain features of left pneumonectomy concerned with the intrapericardial handling of the vessels in this operation.

HISTORICAL BACKGROUND

The first successful pneumonectomies were performed by Nissen,[1] Haight,[2] and Graham and Singer[3] employing the tourniquet technique; however, it was Rienhoff[4] who early advocated the individual dissection, ligation, and division of the hilar structures, and perfected the technique[5] used by most surgeons today in performing the standard pneumonectomy.

Consistent with the general principles of cancer surgery, en bloc dissection of the tumor and surrounding involved structures should be effected in operations for cancer of the lung. Credit for extending the limits of dissection in pneumonectomy to include the intrapericardial portion of the vessels and mediastinal nodes goes to Allison.[6] He first described the technique in 1946, stressing the fact that tissues should be removed in continuity. Later, in discussing a paper by Churchill and co-workers,[7] he stated that "to do either a lobectomy or a pneumonectomy and then pick out isolated glands from the mediastinum is to forget our surgical pathology." While in 1942 his extrapericardial dissections outnumbered the intrapericardial ones 6 to 1, in 1949, 23 out of 27 pneumonectomies were radical resections in which a portion of the pericardium was excised. Of interest also was that during this period, his operative mortality rate dropped from 23 per cent to 4 per cent.

In this country, Gibbon and co-workers[8] were the first to stress the merits of intrapericardial ligation and division of the vessels when dealing with bronchiogenic carcinoma. In 10 out of 20 reported pneumonectomies,[8] such a procedure was essential if the lesion was to be resected at all. In a later communication, Healey and Gibbon[9] reported 44 out of 102 pneumonectomies

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performed by this technique and discussed their findings on intrapericardial anatomy based on dissections of 185 adult cadavers. Other recent reports[10, 11] have mentioned the usefulness of intrapericardial dissection.

INDICATIONS

There are two instances in which it seems mandatory that the surgeon enter the pericardial sac for the securing of the pulmonary vessels if he is to effect left pneumonectomy. The first exists in cases in which the carcinoma has extended in such a fashion as to render extremely hazardous or impossible the securing of the pulmonary artery or of the pulmonary veins outside the pericardium in the usual fashion. The second situation pertains in cases of carcinoma of the lung in which the involvement has progressed so that there are nodes and tissues involved overlying the pulmonary artery or perhaps along the inferior pulmonary vein or along the mediastinum medial to the left main bronchus and behind the heart. The tissues at these sites cannot be adequately excised en bloc by the standard left pneumonectomy. However, it has been our experience that these tissues can be radically and accurately excised along with the lung by securing the pulmonary vessels within the pericardium, and by excising a portion of the pericardium along with the tissues overlying the aortic arch and pulmonary artery and those lying behind the pericardium.

There remain many cases of carcinoma of the lung in which it is technically feasible to remove the lung without entering the pericardium. Nonetheless, by entering it, a more extensive removal of tissue is possible. There is not yet sufficient evidence to permit a conclusion as to whether such an approach is advisable in all operations for bronchiogenic carcinoma. At present, it is our belief that in peripheral carcinoma of the lung without nodal involvement, lobectomy is indicated. If the lesion is centrally located, but small and without local extension or significant involvement of lymph nodes, pneumonectomy without intrapericardial dissection is probably advisable. However, if there is any degree of local invasion or if there is considerable nodal involvement, a more radical pneumonectomy such as will be described is believed by us to be advisable. We recognize that such an extended operation may become advisable for all centrally located carcinomas of the lung when further data regarding mortality and curability become available.

TECHNIQUE

For intrapericardial dissection of the pulmonary vessels on the left side, the pericardium is incised over the region of the left atrial appendage; this incision often is made just posterior to the left phrenic nerve. If there is considerable invasion of the pericardium, the incision is made anterior to the phrenic nerve to allow a more generous excision of it (Fig. 1). The incision is carried cephalad to such a point that the pulmonary artery and aorta are widely exposed. From the lower angle of the pericardial incision and at a right angle to it, an incision is made posteriorly, and wide exposure of the pulmonary artery and superior and inferior pulmonary veins is obtained. The

superior pulmonary vein is dissected out and doubly ligated flush with the left atrial wall and divided. The inferior pulmonary vein is similarly treated, again ligating it flush with the left atrial wall.

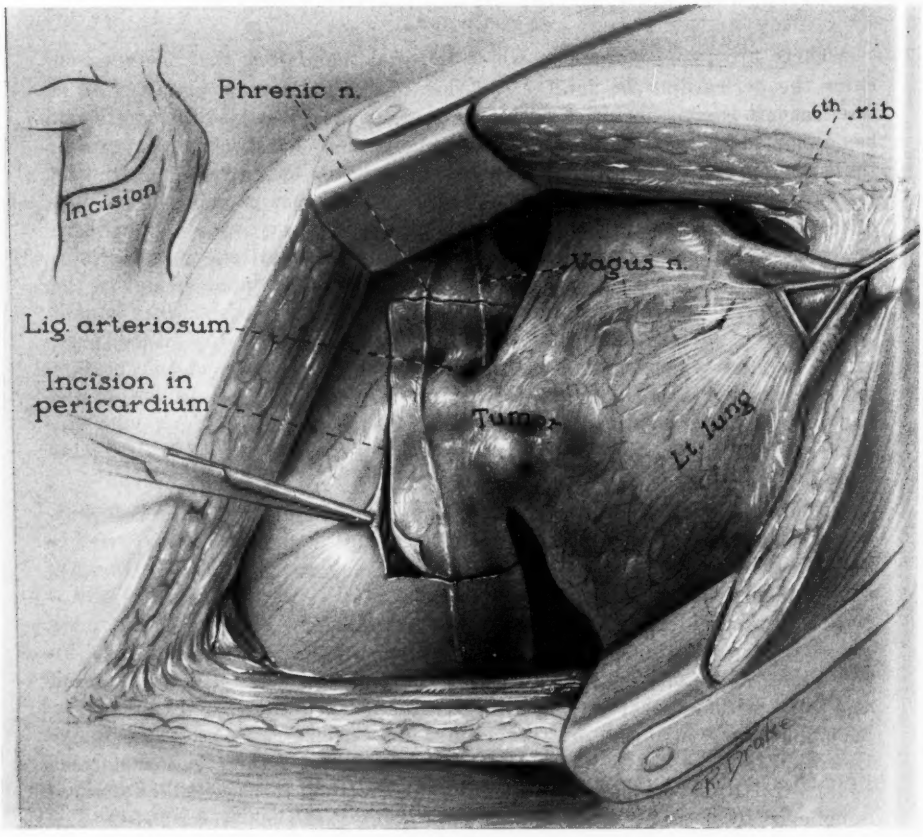

Fig. 1.—Intrapericardial dissection. Initial incision in the pericardium and mediastinal pleura. On occasions when the tumor does not invade tissue near the phrenic nerve, the incision may be made just posterior to the phrenic nerve in order to preserve it.

Next, the left pulmonary artery is dissected out and completely mobilized up to the ligamentum arteriosum. The artery is then doubly or triply ligated just distal to the ligamentum arteriosum and divided. During the mobilization of the pulmonary artery, it is important to sweep all the overlying pericardium and soft tissues including the lymph nodes back toward the lung so as to obtain a wide resection of them (Fig. 2).

The dissection is then carried cephalad over the aortic arch, sweeping all the soft tissues and lymph nodes in this region down with the resected specimen. It is usually necessary in this maneuver to sacrifice the vagus nerve. Usually, but not always, this can be done distal to the origin of the recurrent

laryngeal nerve. The soft tissues in the angle between the bronchus posteriorly and the pulmonary artery anteriorly are all included in the resection.

Once the pulmonary artery has been divided and a portion of the pericardium at this site swept back toward the lung, it becomes possible to include with the resection the peribronchial lymph nodes and subcorynal nodes. Posteriorly and inferiorly, the lymph nodes along the bronchus are likewise swept down to be included along with the resected specimen (Fig. 3). The bronchus is secured about 4 mm. from the coryna and is closed with interrupted silk sutures after the method of Sweet.[12] By careful and accurate dissection, the lung is then peeled away from the mediastinum, great pains being taken to include a wide excision of the soft tissues overlying the aorta and esophagus which include, of course, a number of mediastinal lymph nodes.

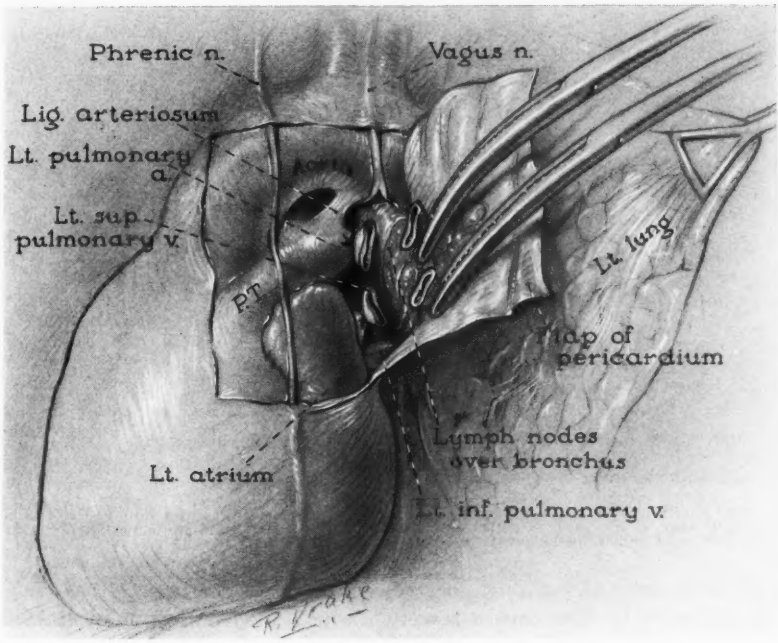

Fig. 2.—Further stage in intrapericardial dissection. In practice, the phrenic nerve is resected along with the pericardial flap in a case such as this, but in order to clarify relations it has been left in situ in this figure and in Fig. 3.

At the end of the resection, there is a defect in the pericardium that sometimes measures 6 to 7 cm. in diameter. We have as yet seen no ill effect from leaving this defect. A flap of pleura is turned down to cover the bronchial stump. The thoracic wall is closed in layers. Drainage is not employed.

COMMENT

There exists at the present time a wide disparity in the views held by surgeons concerning the extirpative treatment of malignant lesions. There are those surgeons who feel that extended operations for carcinomas of bor-

derline operability are not wise and that very few if any patients will be benefited permanently by such procedures. There are others who feel that radical extensive operations should be done not only for carcinomas of borderline operability but for all carcinomas. There are excellent arguments for both schools of thought and it is impossible at this time to state dogmatically that one or the other is correct.

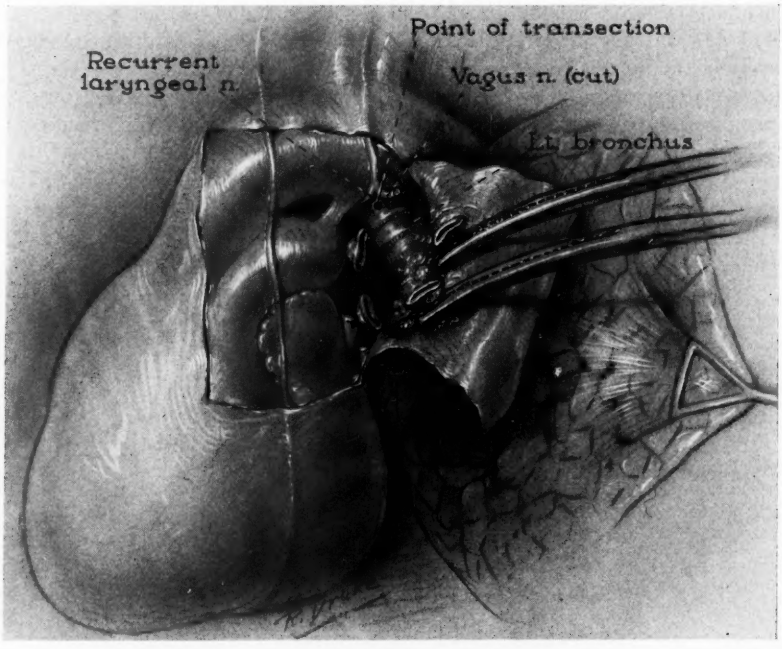

Fig. 3.—Still later stage in intrapericardial dissection. Note that the nodes and soft tissues have been swept down from the upper reaches of the left main bronchus, in preparation for transection of this bronchus just distal to the coryna.

In most cases of centrally located carcinoma of the lung, it has seemed to us advisable to carry out a resection which is somewhat more extensive than the standard pneumonectomy. On the left side, this implies not only ligation of the pulmonary vessels within the pericardium but also wide removal of a portion of the pericardium and all the lymph nodes surrounding the extrapericardial portions of these vessels. It implies also wide removal of the soft tissues beneath the aortic arch and all the lymph nodes going up along the left main bronchus to the coryna. It implies high division of the left main bronchus so as to get well above the carcinoma.

It is our opinion that such an extended pneumonectomy should offer most patients requiring the operation some better hope of cure than the traditional operation in which admittedly many mediastinal lymph nodes that could be removed by the more extended procedure are left behind. Furthermore, there

is little question that certain lesions which would be inoperable because of the involvement around the pulmonary vessels become, in truth, operable if one is willing to proceed with intrapericardial dissection.

The extended operation has been carried out by many individuals as well as by ourselves without a significant increase in the risk of the operation. Our experience is relatively small; we have performed intrapericardial dissection on the left side in only 18 cases. In this group, there have been no complications of any kind, save a single fatal one. In this case, the operation proceeded satisfactorily and the patient's condition was good for about two hours after the operation. Massive hemorrhage then occurred into the left side of the thorax, and at re-exploration we found the ligatures had become dislodged from the central end of the pulmonary artery. Bleeding was controlled but the patient suffered such a prolonged period of cerebral anoxia that he succumbed within twenty-four hours. This complication was probably the result of a technical error, the occurrence of which can be minimized by extreme care in the handling of the vessels.

SUMMARY

The advantages and technique of radical left pneumonectomy employing intrapericardial dissection of the vessels are presented. It is emphasized that by this technique a more radical resection of possible cancer-bearing tissue is effected. Furthermore, certain lesions which would be inoperable because of involvement around the pulmonary vessels become operable when intrapericardial dissection is employed.

REFERENCES

1. Nissen, R.: Exstirpation eines ganzen Lungenflügels, Zentralbl. f. Chir. **58**: 3003-3006, 1931.
2. Haight, Cameron: Total Removal of Left Lung for Bronchiectasis, Surg., Gynec. & Obst. **58**: 768-780, 1934.
3. Graham, E. A., and Singer, J. J.: Successful Removal of an Entire Lung for Carcinoma of the Bronchus, J. A. M. A. **101**: 1371-1374, 1933.
4. Rienhoff, W. F., Jr.: Pneumonectomy: A Preliminary Report of the Operative Technique in Two Successful Cases, Bull. Johns Hopkins Hosp. **53**: 390-393, 1933.
5. Rienhoff, W. F., Jr.: The Present Status of the Surgical Treatment of Carcinoma of the Lung, Ann. Surg. **125**: 541-565, 1947.
6. Allison, P. R.: Intrapericardial Approach to the Lung Root in the Treatment of Bronchial Carcinoma by Dissection Pneumonectomy, J. THORACIC SURG. **15**: 99-117, 1946.
7. Churchill, E. D., Sweet, R. H., Soutter, L., and Scannell, J. G.: Surgical Management of Carcinoma of Lung; Study of Cases Treated at Massachusetts General Hospital From 1930 to 1950, J. THORACIC SURG. **20**: 349-358, 1950.
8. Gibbon, J. H., Jr., Clerf, L. H., Herbut, P. A., and DeTuerk, J. J.: The Diagnosis and Operability of Bronchiogenic Carcinoma, J. THORACIC SURG. **17**: 419-427, 1948.
9. Healey, J. E., Jr., and Gibbon, J. H., Jr.: Intrapericardial Anatomy in Relation to Pneumonectomy for Pulmonary Carcinoma, J. THORACIC SURG. **19**: 864-874, 1950.
10. Boyd, D. P.: A More Radical Total Pneumonectomy, S. Clin. North America **31**: 823-826, 1951.
11. Curtillet, E., and Houel, J.: Pneumonectomie pour cancer bronchique, par voie d'abord transpéricardique du pédicle, Afrique franç. chir. pp. 257-259, 1947.
12. Sweet, R. H.: Closure of Bronchial Stump Following Lobectomy or Pneumonectomy, Surgery **18**: 82-84, 1945.

RESPIRATORY ACIDOSIS DURING INTRATHORACIC SURGERY: THE (OVERHOLT) PRONE POSITION

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RESPIRATORY acidosis as a complication of thoracic surgery was described as early as 1938 by Crafoord.[3] Quantitative investigations in man by several observers[1, 6, 8] have confirmed this earlier finding that a high arterial blood carbon dioxide tension frequently occurs during intrathoracic pulmonary resection, but they are not in agreement as to the mechanisms that impede the excretion of carbon dioxide. Taylor and Roos[13] report that the diminished alveolar ventilation is caused by the depressant effect of ether anesthesia on the respiratory center. Gibbon and associates[6] state that the acidosis is a result of inadequate pulmonary ventilation, caused by an open pneumothorax and not by the lateral position. Beecher and his associates[2] report that the accumulation of carbon dioxide in the blood during surgery of the open thorax is related to the position of the patient, and that the prone (Overholt) and supine positions are the most favorable for the excretion of carbon dioxide (unassisted respiration).

It seemed that further studies might elucidate the causes of respiratory acidosis during thoracic surgery. If, as Beecher states, the prone position is the most favorable for the excretion of carbon dioxide during intrathoracic surgery, analysis of the variables that may disturb the acid-base balance during anesthesia and surgery would help clarify the mechanisms involved in producing high CO_2 tensions in the blood. In order to evaluate fully the effect of the Overholt prone position on carbon dioxide excretion during pulmonary surgery, such variables as preoperative sedation, depth of ether anesthesia, change of position, opening of the pleural cavity, and pulmonary resection have been serially analyzed in this study.

Factual data are presented to show that high carbon dioxide tension occurs in the prone position, with respiration neither assisted nor controlled. The open thorax and the depth of ether anesthesia are the two most important factors in producing a respiratory acidosis during pulmonary surgery.

PREOPERATIVE SEDATION, ANESTHETIC TECHNIQUES, AND AGENTS

Sedation.—All patients in this series received 0.1 Gm. pentobarbital sodium, subcutaneously, two hours before induction of anesthesia, and one hour later received morphine sulfate (or Demerol) plus scopolamine. The selection and

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dosage of morphine or Demerol varied according to the patient's age, sex, and physical status. The dose of scopolamine was 0.6 mg., morphine ranged from 6 to 10 mg., and Demerol from 25 to 100 mg.

Anesthesia.—Ether-oxygen was the maintenance anesthetic agent. The patients were divided into two groups, according to the depth of anesthesia: Group I, light-ether anesthesia; Group II, moderate-depth anesthesia. In Group I endotracheal intubation was performed under topical laryngotracheal 5 per cent cocaine anesthesia. General anesthesia was induced with a 2.5 per cent intravenous solution of Pentothal sodium after the patient was placed in the prone position. Anesthesia was maintained in a very light plane with ether and oxygen. Eyelid reflexes and eyeball movement were active throughout the procedure. The patient periodically reacted to painful stimuli by movement of legs or arms. In Group II, while the patient was in the supine position, general anesthesia was induced with nitrous oxide and oxygen and maintained with ether-oxygen. The muscular relaxation obtained permitted endotracheal intubation and the patient was placed in the prone position. A moderate plane of the surgical stage of ether anesthesia was maintained throughout the operative procedure.

Anesthesia Technique.—An imbedded Latex endotracheal tube with inflatable cuff was connected in series with a to-and-fro Waters' canister and bag. The endotracheal balloon was inflated to obtain an airtight fit. The to-and-fro canister was filled with fresh Baralyme in each case and changed every hour. Respirations were spontaneous throughout the entire anesthetic and surgical procedure and the patient's respiratory exchange was neither assisted nor controlled at any time.

The depth of anesthesia of the patients in Group I is identified in Table I by the letter "L" and in Group II by the letter "D."

Position.—The patient was placed face-down on an Overholt-Compere table,[9] positioned so that the crest of the ilium was supported by the edge of the operating table and the chest by an adjustable pad placed at the cephalad third of the sternum. This allowed the chest cage to expand freely. The head was supported by a modified cerebellar headrest.

General Methods.—The acid-base equilibrium was studied in twenty-three patients. Twenty-two patients were anesthetized with ether; one patient had a pneumonectomy under paravertebral procaine 1 per cent block with endotracheal oxygen. Ninety-six serial acid-base analyses were obtained.

Arterial blood samples were drawn in the following sequence: (1) before the administration of the preoperative sedation, (2) sixty minutes after the administration of the preanesthetic sedation, (3) after the patient was placed in the prone position and anesthetized, (4) before the pleura was opened, (5) after the pleura was opened, before the lobe or lung had been removed, (6) after lobectomy or pneumonectomy with the pleura still open, and (7) at the conclusion of the operation.

Respiratory studies of the tidal exchange, respiratory rate, and respiratory minute volume were obtained by connecting a balanced-type Benedict-Roth spirometer directly to the endotracheal tube. Measurements were made with the patient in the supine and prone positions during the operative procedure.

One medical staff anesthetist administered the anesthesia to all patients studied during this investigation. All patients were operated on by one surgeon.*

Chemical Methods.—Blood was drawn from the femoral artery before the administration of the preanesthetic medication. A Cournand needle was inserted into the radial artery and taped to the wrist with adhesive plaster strips before induction of anesthesia. Arterial blood for oxygen and carbon dioxide determinations was collected by slightly heparinized syringes and transferred to oxalated tonometers over mercury. Arterial blood for pH was collected under oil and centrifuged. The pH of the serum was determined by a Beckman model G glass electrode. This instrument was standardized before and after each determination with a standard buffer solution having a pH of 7.00. The pH was corrected for a temperature of 38° C.[4]

The arterial oxygen content, oxygen capacity, and carbon dioxide content determinations were made on 1 c.c. samples of whole blood by the method of Van Slyke and Neill. The Goldstein modification of the Van Slyke method was used when ether was present in the blood.[7] Carbon dioxide tension was calculated from the carbon dioxide content in volumes per cent, and pH value from the nomogram of Peters and Van Slyke.[10] Values higher than could be read from the nomogram were calculated by the Henderson-Hasselbalch equation. Total CO_2 values in millimols per liter were read from the chart of Peters and Van Slyke.[11] The bicarbonate value of the plasma $[(HCO_3^-)_p]$ was calculated. The calculated data depend mainly on accurate determinations of the pH. In order to obtain accurate determinations within the narrowest margin of error, the analyses of blood gases and pH were all performed by one individual expertly trained in these techniques.

RESULTS

The composite data of the investigation are given in Table I.

The effect of preoperative sedation on the arterial blood carbon dioxide and oxygen saturation is listed in Tables II and III. Analysis of these tables indicates that preoperative sedation in some instances may produce retention of carbon dioxide (see Table II). From Table III it can be seen that moderate doses of pentobarbital with morphine and scopolamine do not cause respiratory acidosis in most patients. Statistical analysis of Table II shows that the T test for examination of the significance in differences in pCO_2 before and after sedation gives the value $T = 4.44$, with 7 degrees of freedom. This value is significant at the .01 significance level. In Table III the observation of the effect of sedation in eighteen patients reveals a correlation coefficient between "time after sedation" and pCO_2 of $-.27$. This figure indicates that

*Dr. Francis Woods.

TABLE I. ACID-BASE EQUILIBRIUM, THORACIC ANESTHESIA, (OVERHOLT) PRONE POSITION, SPONTANEOUS RESPIRATION

CASE	AGE	SEX	MEDICATION		DIAGNOSIS AND OPERATION	ANESTHESIA			POSITION	PLEURA OPEN (MIN.)		pH_a 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM./L)	(HCO_3^-) (mM./L)	HGB. (GM./100)	β	(HCO_3^-) CORRECTED TO pH 7.4 (mM./L)	CHANGE IN FIXED ACID	BLOOD O_2 SAT. (%)
			MORPH. (MG.)	SCOP. (MG.)		CONDITIONS	TIME (MIN.)	DEPTH		(MIN.)										
1	28	F	8.1	0.324	A-V aneurysm	Control			Supine			7.45	28	19.8	18.9	14.7	28.8	20.4		89
						Post-sed.	60		Supine			7.19	50	19.5	18.0	14.7	28.8	11.9	+ 8.5	89
					Lobectomy	Ether/Oxygen	105	D	Prone	110	35	7.00	82	20.6	18.1	14.7	28.8	6.6	+13.8	81
2	28	F	11.0	0.432	Tuberculosis	Control			Supine			7.42	34	22.0	21.0	10.1	22.4	21.2		97
						Post-sed.	60		Supine			7.21	52	21.4	19.8	10.7	23.3	15.4	+ 5.8	95
					Lobectomy	Ether/Oxygen	40	L	Prone	65		7.43	30	20.0	19.1	10.7	23.3	19.8	+ 1.4	98
3	48	F	11.0	0.432	Brochiectasis	Control			Supine			7.43	41	27.1	25.9	14.1	27.9	26.7		92
						Post-sed.	87		Supine			7.31	50	24.7	23.2	13.9	27.7	20.7	+ 6.0	87
					Pneumonectomy	Ether/Oxygen	10		Supine			7.23	64	26.6	24.7	14.0	27.9	20.0	+ 6.7	90
						Ether/Oxygen	70		Prone	45		7.30	56	27.0	25.3	14.0	27.9	22.5	+ 4.2	92
						Ether/Oxygen	132	D	Prone	107	52	7.08	109	34.1	30.8	14.0	27.9	21.9	+ 4.8	79
4	48	M	11.0	0.432	Lipoma	Control						7.39	43	25.6	24.3	14.7	28.8	24.0		99
						Post-sed.	45					7.31	54	27.0	25.4	14.7	28.8	22.8	+ 1.2	96
					Thoracotomy	Ether/Oxygen	15		Supine			7.33	54	28.4	26.8	14.7	28.8	24.8	− 0.8	100
						Ether/Oxygen	60	L	Prone	40	5	7.36	43	24.2	22.9	14.7	28.8	21.8	+ 2.2	100
5	50	M	11.0	0.432	Carcinoma	Control			Supine			7.30	47	22.9	21.5	11.3	24.1	19.1		90
						Post-sed.	60		Supine			7.21	52	21.3	19.7	11.8	24.9	15.0	+ 4.1	93
					Pneumonectomy	Post-sed.	95		Supine			7.40	31	19.6	18.7	11.8	24.9	18.7	+ 0.4	98
						Post-sed.	110		Prone	15		7.37	34	20.0	19.0	11.8	24.9	18.2	+ 0.9	98
						Ether/Oxygen	60		Prone	105	15	7.03	83	22.0	19.5	13.3	26.9	9.6	+ 9.5	89
						Ether/Oxygen	150	D	Prone	195	105	7.14	72	24.3	22.1	13.3	26.9	15.1	+ 4.0	90
6	56	F	8.1	0.324	Carcinoma	Control						7.35	42	23.5	22.2	11.7	24.7	21.0		89
						Post-sed.	75					7.31	44	22.3	21.0	11.7	24.7	18.8	+ 2.2	93
					Pneumonectomy	Ether/Oxygen	35		Supine			7.25	54	23.8	22.2	11.7	24.7	18.5	+ 2.5	97
						Ether/Oxygen	85		Prone	45		7.35	37	20.6	19.5	11.6	24.5	18.3	+ 2.7	93
						Ether/Oxygen	130	D	Prone	90	40	7.10	76	23.6	21.3	12.3	25.5	13.7	+ 7.3	96
7	63	M	75.0 (Dem.)	0.324	Carcinoma	Control						7.41	45	28.5	27.1	13.9	27.7	27.4		92
						Post-sed.	65		Supine			7.21	66	25.9	23.9	13.9	27.7	18.7	+ 8.7	90
					Pneumonectomy	Ether/Oxygen	90		Supine			7.23	69	28.5	26.4	13.9	27.7	21.7	+ 5.7	100
						Ether/Oxygen	140		Prone	40		7.21	76	30.0	27.7	13.9	27.7	22.5	+ 4.9	96
						Ether/Oxygen	175		Prone	75	25	7.09	96	31.0	28.1	13.9	27.7	19.5	+ 7.9	95
						Ether/Oxygen	235	D	Prone	135	85	7.03	115	33.0	29.5	13.9	27.7	19.3	+ 8.1	100

TABLE I—CONT'D

CASE	AGE	SEX	MEDICATION		DIAGNOSIS AND OPERATION	ANESTHESIA			POSITION	(MIN.)	PLEURA OPEN (MIN.)	pH_s 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (MM./L.)	(HCO_3^-) (MM./L.)	HGB. (GM./100)	β	(HCO_3^-) CORRECTED TO pH 7.4 (MM./L.)	CHANGE IN FIXED ACID	BLOOD O_2 SAT. (%)
			MORPH. (MG.)	SCOP. (MG.)		CONDITIONS	TIME (MIN.)	DEPTH												
8	75	M	5.4	0.432	Carcinoma	Control						7.36	46	25.3	23.9	13.6	27.2	22.8		91
						Post-sed.	60		Supine			7.23	62	26.0	24.1	12.4	25.6	19.8	+ 3.0	88
					Pneumonectomy	Post-sed.	105		Supine			7.33	48	25.0	23.6	12.4	25.6	21.8	+ 1.0	89
						Oxygen			Prone	10		7.20	62	25.0	23.1	12.4	25.6	18.0	+ 4.8	93
						Oxygen			Prone	60	35	7.13	70	23.4	21.3	12.4	25.6	14.4	+ 8.4	97
						Oxygen		L	Prone	120	95	7.21	60	27.6	25.8	12.4	25.6	21.0	+ 1.8	90
9	20	M	11.0	0.432	Tuberculosis	Post-sed.	75		Supine			7.34	50	26.4	24.9	16.7	31.6	23.0		96
						Ether/Oxygen	49		Prone	54		7.05	74	21.8	19.6	16.5	31.3	8.7	+14.3	99
					Lobectomy	Ether/Oxygen	100		Prone	105	50	6.99	86	22.7	20.1	15.7	30.3	7.7	+15.3	98
						Ether/Oxygen	178	D	Prone	183	128	7.02	83	21.6	19.1	16.6	31.4	7.2	+15.8	93
10	36	F	50.0 (Dem.)	0.324	Tuberculosis	Post-sed.	75		Supine			7.28	52	23.9	22.3	13.7	27.5	19.0		86
						Control			Prone	10		7.37	41	24.6	23.4	13.7	27.5	22.6	− 3.6	93
					Lobectomy	Ether/Oxygen	35		Prone	60		7.45	35	24.2	23.2	13.7	27.5	24.5	+ 5.5	92
						Ether/Oxygen	65	L	Prone	90	25	7.28	50	23.6	22.1	13.7	27.5	18.8	+ 0.2	88
11	43	M	11.0	0.432	Bronchiectasis	Post-sed.	45		Supine			7.39	46	27.4	26.0	14.5	28.5	25.7		91
						Ether/Oxygen	50		Prone	50		7.15	70	24.3	22.2	14.6	28.6	15.1	+10.6	94
					Lobectomy	Ether/Oxygen	103		Prone	103	15	7.27	64	28.8	26.9	15.2	29.6	23.1	+ 2.6	84
						Ether/Oxygen	210	D	Prone	210	122	7.07	97	30.3	27.4	15.1	29.3	17.7	+ 8.0	98
						Control			Supine			7.31	52	26.0	24.4	14.6	28.6	21.8	+ 3.9	80
12	43	F	8.1	0.324	Bronchiectasis	Post-sed.	55		Supine			7.42	40	25.7	24.5	12.0	25.1	25.0		95
						Ether/Oxygen	50		Prone	30		7.25	72	25.2	23.0	12.5	25.8	19.1	+ 5.9	95
					Lobectomy	Ether/Oxygen	95		Prone	75	32	7.23	60	24.8	23.0	12.2	25.5	18.7	+ 6.3	91
						Ether/Oxygen	165	D	Prone	145	102	7.18	66	24.6	22.6	12.9	26.4	16.8	+ 8.2	94
						Control						7.24	57	24.5	22.8	12.4	25.6	18.7	+ 6.3	92
13	44	M	11.0	0.432	Tuberculoma	Post-sed.	75		Supine			7.42	40	25.5	24.3	14.6	28.7	23.7		98
						Ether/Oxygen	40	D	Prone	50	10	7.34	48	25.6	24.2	14.6	28.7	22.5	+ 1.2	
					Thoracotomy	Control			Supine			7.20	62	24.7	22.8	14.2	28.1	17.2	+ 6.5	92

14	51	M	11.0	0.432	Carcinoma	Post-sed.	85		Supine			7.55	22	20.0	19.3	13.7	27.4	23.4		91
						Post-sed.	95		Prone	10		7.61	19	19.7	19.1	13.7	27.4	24.9	− 1.5	95
					Pneumonectomy	Ether/Oxygen	23	L	Prone	63	13	7.37	45	25.6	24.3	13.7	27.4	23.5	− 0.1	96
						Post-op.	225		Supine			7.43	40	26.2	25.0	13.7	27.4	25.8	− 2.4	87
15	54	M	8.1	0.432	Adenoma	Post-sed.	75		Supine			7.40	41	25.0	23.8	14.1	28.0	23.8		92
						Ether/Oxygen	30		Prone	45		7.17	56	20.5	18.8	13.5	27.2	12.6	+11.2	93
					Lobectomy	Ether/Oxygen	50		Prone	65	17	7.38	36	21.3	20.2	13.9	27.8	19.7	+ 4.1	92
						Ether/Oxygen	122		Prone	137	89	7.24	52	22.1	20.5	13.5	27.2	16.2	+ 7.6	91
						Control			Supine			7.38	37	21.8	20.7	12.9	26.4	20.2		91
16	73	F	4.0	0.324	Bronchiectasis	Post-sed.	85		Supine			7.50	26	20.5	19.7	12.1	25.3	22.2		90
						Control			Prone	10		7.52	21	17.7	17.1	12.1	25.3	20.1	+ 2.1	90
					Lobectomy	Ether/Oxygen	22		Prone	37		7.42	37	24.0	22.9	12.1	25.3	24.9	− 2.7	95
						Ether/Oxygen	35	L	Prone	50	10	7.21	56	22.8	21.1	12.1	25.3	16.3	+ 5.9	87
17	66	M	35.0 (Dem.)	0.324	Carcinoma	Post-sed.	60		Supine			7.30	51	25.1	23.6	12.5	25.8	21.0		94
						Ether/Oxygen	36		Prone	51		7.38	47	27.0	25.6	11.8	24.8	25.1	− 4.1	98
					Thoracotomy	Ether/Oxygen	72		Prone	87	32	7.35	47	25.5	24.1	12.8	26.3	22.8	− 1.8	96
						Ether/Oxygen	132	L	Prone	147	92	7.48	33	23.8	22.9	13.0	26.5	25.0	− 4.0	97
						Control			Supine			7.51	29	23.0	22.1	13.0	26.5	25.0	− 4.0	84
18	70	F	50.0 (Dem.)	0.324	Bronchiectasis	Post-sed.	80		Supine			7.34	52	27.6	26.0	12.6	25.8	24.5		95
						Ether/Oxygen	52		Prone	12		7.33	50	25.9	24.4	13.9	27.8	22.5	+ 2.0	96
					Lobectomy	Ether/Oxygen	85	D	Prone	45	14	7.04	89	26.0	23.3	13.5	27.0	13.6	+10.9	92
						Control			Supine			7.16	75	26.5	24.2	12.5	25.8	18.0	+ 6.5	88
19	67	M	25.0 (Dem.)	0.324	Carcinoma	Ether/Oxygen	10		Supine			7.17	78	28.5	26.2	10.6	23.1	20.9		91
						Ether/Oxygen	47		Prone	17		7.17	78	28.0	25.7	10.6	23.1	20.4	+ 0.5	89
					Pneumonectomy	Ether/Oxygen	76	D	Prone	46	16	7.02	114	29.6	26.2	10.6	23.1	17.3	+ 3.6	78
20	59	M	8.1	0.324	Bronchial fistula	Ether/Oxygen	9		Prone	54		7.33	45	23.4	22.1	14.5	28.6	20.1		95
					Thoracotomy	Ether/Oxygen	33	D	Prone	78	18	7.09	86	27.8	25.2	14.5	28.6	16.3	+ 3.8	
21	55	M	8.1	0.324	Carcinoma	Ether/Oxygen	20		Prone			7.21	43	17.8	16.5	10.8	23.5	12.1		
						Ether/Oxygen	53	L	Prone		28	7.31	50	25.0	23.5	14.5	28.5	20.9	− 8.8	89
					Thoracotomy	Control						7.39	39	23.3	22.1	15.3	29.7	21.8	− 9.7	86
22	43	F	8.1	0.432	Bronchiectasis	Ether/Oxygen	45		Prone	65		7.23	43	18.5	17.2	13.2	26.8	12.7		99
						Ether/Oxygen	95		Prone	115	45	7.37	32	19.0	18.0	13.4	27.1	17.2	− 4.5	86
					Lobectomy	Ether/Oxygen	115		Prone	135	65									
						Ether/Oxygen	120	L	Prone	140	70	7.36	35	20.4	19.4	13.8	27.6	18.3	− 5.6	83
23	60	M	8.1	0.324	Carcinoma	Ether/Oxygen	50		Prone	55		7.07	92	28.7	25.9	12.8	26.2	17.3		98
					Pneumonectomy	Ether/Oxygen	110	D	Prone	115	35	7.31	57	28.4	26.7	12.8	26.2	24.4	− 7.4	83

TABLE II. EFFECT OF SEDATION

		BEFORE				SECOND SEDATION		AFTER			
CASE	AGE	pH_s 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %	M.S. (MG.)	SCOP. (MG.)	pH_s 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %
1	28	7.45	28	19.8	89	8.1	0.324	7.19	50	19.5	89
2	28	7.42	34	22.0	97	11.0	0.432	7.21	52	21.4	95
3	48	7.43	41	27.1	92	11.0	0.432	7.31	50	24.7	87
4	48	7.39	43	25.6	99	11.0	0.432	7.31	54	27.0	96
5	50	7.30	47	22.9	90	11.0	0.432	7.21	52	21.3	93
6	56	7.35	42	23.5	89	8.1	0.324	7.31	44	22.3	93
7	63	7.41	45	28.5	92	75.0 (Dem.)	0.324	7.21	66	25.9	90
8	75	7.36	46	25.3	91	5.4		7.23	62	26.0	88
Avg.	49.5	7.39	40.7	24.3	92.4	9.4 (M.S.)	0.385	7.25	53.8	23.5	91.4

there may be a slight decrease in CO_2 tension with an increase in time. A confidence interval, based on all eighteen observations for the average of pCO_2 mm. Hg, is $41.8 = 52.6$. These observations do not rule out the possibility that they have come from a series in which the normal value for pCO_2 is 44 mm. Hg.

The significance of this evaluation is that the depressant effects of sedation on respiration are not predictable in patients with pulmonary lesions requiring thoracic surgery. These figures indicate that preoperative sedation with pentobarbital plus morphine and scopolamine can cause a retention of carbon dioxide in some patients. The postsedation values for arterial oxygen saturation were within a normal range.

TABLE III. EFFECT OF SEDATION

			SECOND SEDATION		TIME AFTER SEDATION			TOTAL	
CASE	AGE	DIAGNOSIS	M.S. (MG.)	SCOP. (MG.)	(MIN.)	pH_s 38° C.	pCO_2 (MM. HG)	CO_2 (mM/L.)	O_2 SAT. %
1	28	Aneurysm lung	8.1	0.324	60	7.19	50	19.5	89
2	28	Tuberculosis	11.0	0.432	60	7.21	52	21.4	95
3	48	Bronchiectasis	11.0	0.432	135	7.31	50	24.7	87
4	48	Lipoma	11.0	0.432	45	7.31	54	27.0	96
5	50	Carcinoma	11.0	0.432	60	7.21	52	21.3	93
6	56	Carcinoma	8.1	0.324	75	7.31	44	22.3	93
7	63	Carcinoma	75.0 (Dem.)	0.324	65	7.21	66	25.9	90
8	75	Carcinoma	5.4		60	7.23	62	26.0	88
9	20	Tuberculosis	11.0	0.432	75	7.34	50	26.4	96
10	36	Granuloma	50.0 (Dem.)	0.324	75	7.28	52	23.9	86
11	43	Bronchiectasis	11.0	0.432	45	7.39	46	27.4	91
12	43	Bronchiectasis	8.1	0.324	55	7.42	40	25.7	95
13	44	Tuberculoma	11.0	0.432	75	7.42	40	25.5	98
14	51	Carcinoma	11.0	0.432	85	7.55	22	20.0	91
15	54	Adenoma	8.1	0.432	75	7.40	41	25.0	92
16	73	Bronchiectasis	4.0	0.324	85	7.50	26	20.5	90
17	66	Carcinoma	35.0 (Dem.)	0.324	60	7.30	51	25.1	94
18	70	Granuloma	50.0 (Dem.)	0.324	80	7.34	52	27.6	95
Avg.	49.8		9.3 (M.S.)	0.360	69.4	7.328	47.2	24.1	92

TABLE IV. PRONE POSITION (OVERHOLT), CHEST CLOSED

ETHER ANESTHESIA, LIGHT							ETHER ANESTHESIA, SURGICAL STAGE						
CASE	AGE	ANESTHESIA (MIN.)	pH_s 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %	CASE	AGE	ANESTHESIA (MIN.)	pH_s 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %
2	28	40	7.43	30	20.0	98	3	48	70	7.30	56	27.0	92
4	48	15	7.33	54	28.4	100	6	56	85	7.35	37	20.6	93
8	75	60	7.20	62	25.0	93	7	63	140	7.21	76	30.0	96
10	36	35	7.45	35	24.2	92	9	20	49	7.05	74	21.8	99
15	54	30	7.17	56	20.5	93	11	43	50	7.15	70	24.3	94
16	73	22	7.42	37	24.0	95	12	43	50	7.25	72	25.2	95
17	66	36	7.38	47	27.0	98	18	70	52	7.33	50	25.9	96
22	43	45	7.23	43	18.5	100	19	67	47	7.17	78	28.0	89
							20	59	9	7.33	45	23.4	95
							23	60	50	7.07	92	28.7	98
Avg.	53	35	7.33	45.5	23.5	96		52.9	60	7.22	65.0	25.5	94.7

Table IV shows the effect of the light and moderate surgical states of ether anesthesia on the arterial blood and pH_s, carbon dioxide tension, and oxygen saturation, before opening the pleura, with the patient in the prone position. Seven of the ten patients who were in the moderate surgical state of anesthesia had respiratory acidosis; in Case 23, there was an elevated pCO_2 (92 mm. Hg) and a pH of 7.07—a severe respiratory acidosis. In the group of patients who were lightly anesthetized, the highest pCO_2 was 62 mm. Hg, with a pH of 7.20.

Increasing the depth of ether anesthesia, with the patient in the prone position, evidently depresses effective alveolar ventilation as shown by a retention of carbon dioxide.

Analyses of the effects of lobectomy, pneumonectomy, and light and moderate surgical states of ether anesthesia on the excretion of carbon dioxide are shown in Tables V and VI. The observed difference between the average pCO_2

TABLE V. PRONE POSITION (OVERHOLT), CHEST OPEN

LOBECTOMIES							PNEUMONECTOMIES						
CASE	AGE	CHEST OPEN (MIN.)	pH_s 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %	CASE	AGE	CHEST OPEN (MIN.)	pH_s 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %
1	28	35	7.00	82	20.6	81	3	48	55	7.08	109	34.1	79
9	20	50	6.99	86	22.7	98	5	50	105	7.14	72	24.3	90
10	36	25	7.28	50	23.6	88	6	56	40	7.10	76	23.6	96
11	43	122	7.07	97	30.3	98	7	63	85	7.03	115	33.0	100
12	43	105	7.18	66	24.6	94	8	75	95	7.21	60	27.6	90
15	54	90	7.24	52	22.1	91	14	51	13	7.37	45	25.6	96
16	73	10	7.21	56	22.8	87	19	67	16	7.02	114	29.6	78
18	70	14	7.04	89	23.3	92	23	60	35	7.31	57	28.4	83
22	43	70	7.36	35	20.4	83							
Avg.	45.5	58	7.15	68	23.4	90		59	56	7.16	81	28.3	89

TABLE VI. PRONE POSITION (OVERHOLT), CHEST OPEN

ETHER ANESTHESIA, LIGHT								ETHER ANESTHESIA, SURGICAL STAGE							
CASE	AGE	ANESTHESIA (MIN.)	CHEST OPEN (MIN.)	pH, 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %	CASE	AGE	ANESTHESIA (MIN.)	CHEST OPEN (MIN.)	pH, 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	O_2 SAT. %
4	48	60	5	7.36	43	24.2	100	1	28	105	35	7.00	82	20.6	81
8	75	120	95	7.21	60	27.6	90	3	48	135	55	7.08	109	34.1	79
10	36	65	25	7.28	50	23.6	88	5	50	150	105	7.14	72	24.3	90
13	44	40	10	7.34	48	25.6	—	6	56	130	40	7.10	76	23.6	96
14	51	23	13	7.37	45	25.6	96	7	63	235	85	7.03	115	33.0	100
15	54	137	89	7.24	52	22.1	91	9	20	178	128	7.02	83	21.6	93
16	73	35	10	7.21	56	22.8	87	11	43	210	122	7.07	97	30.3	98
17	66	127	92	7.48	33	23.8	97	12	43	165	102	7.18	66	24.6	94
22	43	120	70	7.36	35	20.4	83	19	67	76	16	7.02	114	29.6	78
								20	59	33	18	7.09	86	27.8	—
								23	60	110	35	7.31	57	28.4	83
Avg.	54	81	45	7.32	47	23.9	91.5		49	139	67	7.09	87	27.1	89

of 68 mm. Hg and pH of 7.15 for lobectomies, and the pCO_2 of 81 mm. Hg and pH of 7.16 for pneumonectomies, with pleura open, may well be due to mere sampling fluctuations. The observed difference between the average pCO_2 of 47 mm. Hg and pH of 7.32 for light anesthesia, and the average pCO_2 of 87 mm. Hg and pH of 7.09 for the moderate surgical state of anesthesia, with the pleura open, is highly significant. The variability of pCO_2 values was investigated by a two-way analysis of variance, based on the type of operative procedure and the depth of anesthesia. Table VII is an analysis of the variance.

TABLE VII

SOURCE OF VARIATION	SUM OF SQUARES	D.F.	MEAN SQUARE	F	TABULATED 5%	F 1%
Operation (lobectomy, pneumonectomy)	131.56	1	131.56	0.4		
Anesthesia (light, moderate)	4998.56	1	4998.56	16.0	4.67	9.07
Interaction	7.75	1	7.75			
Individuals	4061.	13	312.4			

The F value for depth of anesthesia is highly significant, whereas the F value for operation is not significant. The T test for the difference of pCO_2 between the light and moderate states of anesthesia gives a value of $T = 2.76$, with 16 degrees of freedom. This is significant at the .05 level.

These figures are evidence that the decrease in excretion of carbon dioxide (the state of respiratory acidosis) is as likely to occur during the procedure of a lobectomy as it is during a pneumonectomy. The analysis of variance demonstrates that during intrathoracic surgery in the prone position, the more significant factor in causing respiratory acidosis is the depth of anesthesia, and not the type of pulmonary resection. From Table VIII it can be seen that there was no significant change in the carbon dioxide tension after the patients were turned from the supine to the prone position.

TABLE VIII. pH AND pCO_2 AFTER ENDOTRACHEAL INTUBATION

EFFECT OF SUPINE AND PRONE POSITIONS BEFORE ANESTHESIA				
	SUPINE		PRONE	
10 PATIENTS	pH_a 38° C.	pCO_2 (MM. HG)	pH_a 38° C.	pCO_2 (MM. HG)
Average	7.41	36	7.41	32
EFFECT OF SUPINE AND PRONE POSITIONS DURING ETHER ANESTHESIA				
	SUPINE		PRONE	
16 PATIENTS	pH_a 38° C.	pCO_2 (MM. HG)	pH_a 38° C.	pCO_2 (MM. HG)
Average	7.24	64	7.27	58

Further analysis does not indicate any relation between the length of time the pleura is open and the excretion of carbon dioxide. The course of the CO_2 tension in eight representative intrathoracic procedures is shown in Fig. 1, from which it is apparent that the length of time the pleura remains open has no bearing on the CO_2 tension. Fig. 2 shows the lack of correlation between the length of time the pleura remains open and CO_2 tension during twenty-three intrathoracic procedures.

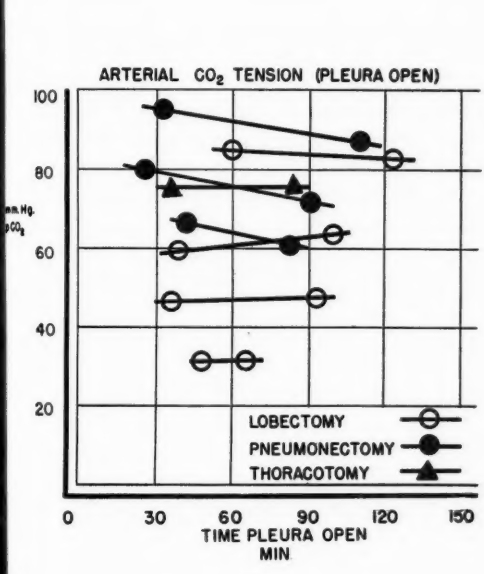

Fig. 1.

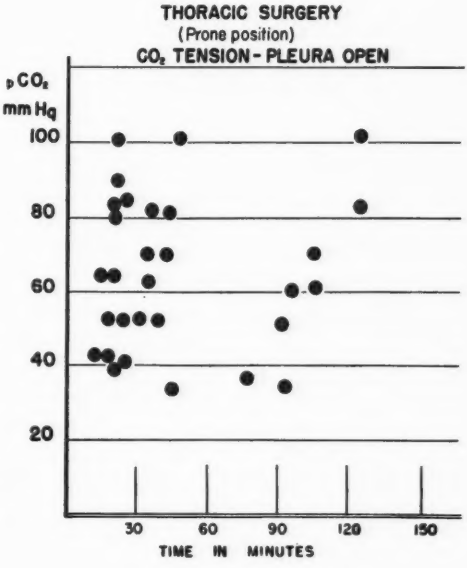

Fig. 2.

Fig. 1.—The figure shows that time had no effect on the arterial pCO_2 while the pleura was open (eight representative intrathoracic procedures).

Fig. 2.—The arterial blood CO_2 tension is plotted against the time the pleura was open (thirty intrathoracic procedures). The figure indicates the lack of correlation between these two factors.

Table IX shows that in twenty-three cases, the average of the fixed acids during ether anesthesia for lobectomy or pneumonectomy was within a normal range of variation (+0.8 to +4.4 mM per liter). In several patients the fixed

TABLE IX. ACID-BASE EQUILIBRIUM, PRONE POSITION

	pH_a 38° C.	pCO_2 (MM. HG)	TOTAL CO_2 (mM/L.)	(HCO_3^-) (mM/L.)	HGB. (GM./ 100)	β	(HCO_3^-) CORRECTED TO pH 7.4	FIXED ACID (mM/L.)
Ether Anesthesia, Light								
Preoperative (supine)	7.36	44.4	23.8	22.8	13.5	27.1	21.2	
Chest closed	7.33	45.5	23.5	22.1	12.8	26.2	20.3	−0.8
Chest open	7.32	47.0	23.9	22.6	13.5	27.2	20.4	−0.9
Ether Anesthesia, Surgical Stage								
Preoperative (supine)	7.30	50.0	24.5	23.0	13.5	25.0	20.4	
Chest closed	7.22	65.0	25.5	23.5	13.5	27.2	18.7	−1.7
Chest open	7.09	87.0	27.1	24.5	13.7	27.4	16.0	−4.4

acids were elevated. This occurred in a few patients who had slight elevations of CO_2 tensions. In other instances, where the CO_2 tensions were extremely high, the fixed acids were not elevated.

DISCUSSION

The results of this study show that the Overholt prone position does not aid in the excretion of carbon dioxide during thoracic surgery. Preoperative sedation, depth of ether anesthesia, and an open pneumothorax are the principal factors that may cause a retention of carbon dioxide tension in the arterial blood. It is recognized that there are other factors in addition to these that may produce an increase in alveolar carbon dioxide tension and a fall in pH during thoracic surgery. Among these are ligation of a bronchus previous to ligation of the pulmonary vessels, an open bronchus during lobectomy or pneumonectomy, circulation of blood through inadequately ventilated pulmonary tissue, impairment of pulmonary and systemic circulation, and diminished blood flow through the lung. When these causes are corrected, the carbon dioxide tension is maintained at the pre-existing level, dependent on the depth of anesthesia.

The arterial carbon dioxide tension is considered to equal the mean of the entire range of alveolar carbon dioxide pressure existing in different parts of the lung and at different movements in the ventilatory cycle.[12] The increase in arterial pCO_2 during intrathoracic surgery can be attributed to decreased alveolar ventilation and to the mixing of blood that has passed through inadequately ventilated alveoli with blood that has passed through the well-ventilated lung. The face-down position is not an aid to the ventilation of the lung exposed to atmospheric pressure during the course of thoracic surgery. The exposed lung can be considered functionless; it acts only as a reservoir for venous blood having a high carbon dioxide tension. When pneumonectomy or lobectomy is performed, the increase in carbon dioxide tension is most likely due to a deficiency in the respiratory ventilating mechanisms.

The opening of the pleura impairs the bellows action of the muscles of respiration. Respiratory studies[5] demonstrate that an open pleura (see Fig. 3) reduces the effective tidal volume and alveolar ventilation. Respirations

decrease in amplitude but increase in rate. The resultant increase in respiratory minute volume does not, however, improve the effective tidal exchange. Although the prone position favors an increase in diaphragmatic excursions, the increase is not sufficient to aid the excretion of carbon dioxide.

The respiratory-stimulant action of ether and the reflex surgical stimulation in the light stage of anesthesia can cause an increase in effective tidal volume and respiratory minute volume. In our series, the group that was lightly anesthetized with ether had respiratory rates ranging from 40 to 50 per minute during surgery. Whether a respiratory rate of this magnitude is physiologically sound is questionable because of the increased work of breathing and exaggerated excursions of the muscle wall, diaphragm, and mediastinum. Surely, excessive respiratory movements must impede a meticulous surgical dissection within the thorax.

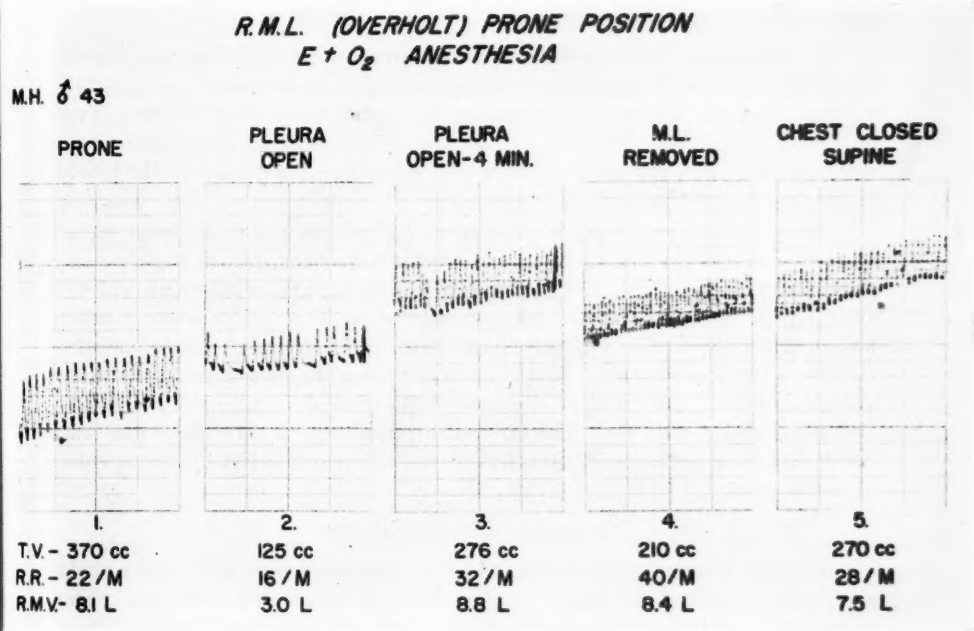

Fig. 3.—Spirogram shows the decrease in effective ventilation during a lobectomy in the prone position.

Comparison of the arterial blood carbon dioxide levels in the group of patients lightly anesthetized and in the group in the midplane of surgical anesthesia demonstrates that it is the depth of ether anesthesia, and not the type of pulmonary resection, that decreases the excretion of carbon dioxide. It can be postulated that in the moderate state of surgical anesthesia the threshold of the respiratory center is elevated and does not respond to reflex surgical stimuli. It is evident that a severe respiratory acidosis may occur during

lobectomy as well as during pneumonectomy. The *effective* respiratory minute volume and *effective* alveolar ventilation are not increased during the surgical state of ether anesthesia when the chest is open. Serial blood gas determinations taken when the pleura was open indicate that the carbon dioxide retention does not increase with time. Analyses of these values are shown in Figs. 1 and 2. Since the alveolar carbon dioxide tension is inversely proportional to alveolar ventilation,[11] it follows that the factors that impair alveolar ventilation are responsible for an elevated pCO_2. If the level of anesthesia is maintained throughout, then the time the pleura is open need not be considered. It is recognized that frequent arterial blood determinations are necessary in order to plot the complete course of the alveolar pCO_2 and correlate it with the etiological factors. A single determination in a single patient, taken when the pleura is open, does not permit a true evaluation. Neither does a comparison of the effect of time in a group of patients, based on single determinations, show any positive correlation.

In this study, the arterial oxygen saturation remained within normal limits after preoperative sedation. This finding is in contrast to a reported[6] average of 88 per cent oxygen saturation of arterial blood after sedation in patients for thoracic surgery; it may be that large doses of depressant drugs were used for premedication, or blood determinations were taken at the height of the depressant effects of the drugs.

The arterial blood oxygen saturation was within a normal range in all but two patients during surgery. The patient in Case 1 had a pulmonary arteriovenous aneurysm, and the respired high oxygen atmosphere did not alter the preoperative arterial oxygen saturation level. The prone position had no influence on the arterial oxygen saturation, in either the nonanesthetized or anesthetized state. Sixteen minutes after the pleura was opened the patient in Case 7 had an arterial oxygen saturation of 78 per cent, pH of 7.02, and pCO_2 of 114 mm. Hg. The lowered arterial oxygen saturation was most likely due to a decrease in alveolar ventilation precipitated by the opening of the pleura.

SUMMARY AND CONCLUSIONS

This has been an evaluation of the etiological factors in respiratory acidosis during thoracic surgery. It has been demonstrated that the prone (Overholt) position does not prevent an increase in carbon dioxide tension during either lobectomy or pneumonectomy.

Dangerously high levels of carbon dioxide tension were encountered when the hemithorax was open and the patients allowed to breathe spontaneously during ether anesthesia. A lowering of the pH and increase in carbon dioxide tension occurred during the surgical state of ether anesthesia, with the patients in the prone position.

Analysis of the effect of lobectomy, pneumonectomy, depth of ether anesthesia, and duration of operation reveals the following: (1) An increase in carbon dioxide tension may occur with the same frequency and severity during

lobectomy as during pneumonectomy; and (2) the severity of the respiratory acidosis is not a factor of time but is a factor of the depth of ether anesthesia during intrathoracic surgery.

Statistical analysis was made by Dr. Gottfried E. Noether, Associate Professor of Mathematics (Statistical Division), Boston University College of Liberal Arts, Boston.

REFERENCES

1. Beecher, H. K., and Murphy, A. J.: Acidosis During Thoracic Surgery, J. THORACIC SURG. **19:** 50-70, 1950.
2. Beecher, H. K., Quinn, T. J., Jr., Bunker, J. P., and d'Alessandro, G. L.: Effect of Position and Artificial Ventilation on the Excretion of Carbon Dioxide During Thoracic Surgery, J. THORACIC SURG. **22:** 135-148, 1951.
3. Crafoord, C.: On the Technique of Pneumonectomy in Man, Tryckeri Aktiebolaget Thule, p. 61, 1938.
4. Cullen, G. E.: Studies of Acidosis XIX. The Colorimetric Determination of the Hydrogen Ion Concentration of Blood Plasma, J. Biol. Chem. **52:** 521, 1922.
5. Etsten, B. E.: To be published.
6. Gibbon, J. H., Jr., Allbritten, F. F., Jr., Stayman, J. W., Jr., and Judd, J. M.: A Clinical Study of Respiratory Exchange During Prolonged Operations With an Open Thorax, Ann. Surg. **132:** 611-625, 1950.
7. Goldstein, Frank, Gibbon, John H., Jr., Allbritten, F. F., Jr., and Stayman, J. W., Jr.: The Combined Manometric Determination of Oxygen and Carbon Dioxide in Blood, in the Presence of Low Concentrations of Ethyl Ether, J. Biol. Chem. **182:** 815-820, 1950.
8. Maier, H. C., Rich, G. W., and Eichen, S.: Clinical Significance of Respiratory Acidosis During Operations, Ann. Surg. **134:** 653-658, 1951.
9. Overholt, R. H., and Woods, F. M.: The Prone Position in Thoracic Surgery, J. Internat. Coll. Surgeons **10:** 216, 1947.
10. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Vol. II: Methods, Baltimore, 1932, Williams & Wilkins Company, 294.
11. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Vol. II: Methods, Baltimore, 1932, Williams & Wilkins Company, 287.
12. Riley, R. L., Lilienthal, J. L., Jr., Proemmel, D. D., and Franke, R. E.: On the Determination of the Physiologically Effective Pressures of Oxygen and CO_2 in Alveolar Air, Am. J. Physiol. **147:** 191-198, 1946.
13. Taylor, F. H., and Roos, A.: Disturbances in Acid-base Balance During Ether Anesthesia, With Special Reference to Changes Occurring During Thoracic Surgery, J. THORACIC SURG. **20:** 289-295, 1950.

A MODIFIED THORACOTOMY TECHNIQUE FOR THE PREVENTION OF POSTOPERATIVE PAIN AND DEFORMITY

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OPERATIONS upon the thoracic cavity may be divided into two groups: those which require collapse of the chest wall, and those which do not. Collapse may be considered necessary in the resectional treatment of pulmonary tuberculosis or to prevent mediastinal shift when the hemithorax is left empty. Otherwise, the resection of ribs is generally done to obtain exposure. In our work, we have felt that removal of a rib increases the difficulty of obtaining airtight closure and often results in a groove in the chest wall along the axis of the resected rib. The importance of this feature was brought forcibly to our attention when a young woman threatened a malpractice suit for a bad cosmetic result, although she admitted that the operation had cured her of bronchiectasis.

In addition, we have been led by our results to believe that, where there is a poor alignment of sectioned ribs and/or excessive movements of the anterior segments, a large callous formation may ensue. If the posterior end of the intercostal nerve becomes entangled in this callus, it may cause the late development of disabling pain. Four of our patients required the operative liberation of the nerve trunk for relief of pain six to eighteen months after resection. These operations were only partially successful.

The standard procedure for posterolateral thoracotomy was laid down as long ago as 1925 by Lilienthal.[1] Later work, particularly by Overholt and Langer,[2] and Klassen,[3] shows that the search for improvement is continuous. Unfortunately, some of the refinements which yield an improvement in results are paid for at a cost of increased operating time. In our work, many methods—those described by the foregoing authors, as well as drilling and diagonal cutting, followed by wiring—were tried and abandoned before the simple method to be described was developed.

It seemed rational to assume that chest deformity could be avoided by conserving, as nearly normal as possible, both the substance and position of the ribs. It also seemed logical to expect that postoperative fixation of the ribs in good position would prevent, to a large extent, the production of excessive callus.

It is our opinion that the thoracotomy technique described here accomplishes these purposes. In all illustrations, the patient is in the face-down position.

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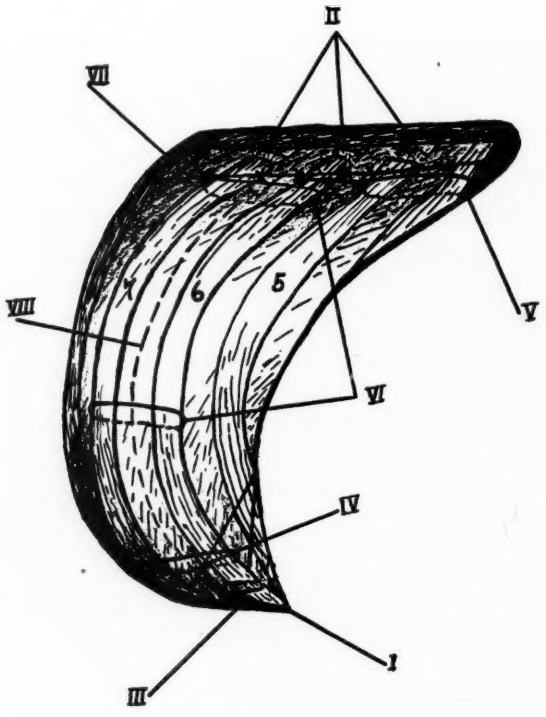
TECHNIQUE

An incision is made, beginning at a point halfway between the fourth dorsal spine and the scapular border, and carried in a curved sweep around the normal position of the angle of the scapula to a point represented by the intersection of the sixth intercostal space and the anterior axillary line. All structures down to the muscles are divided throughout the entire length of this incision. Towels are sutured to the fascia along the margins of the

Fig. 1.—Photograph of anterior angle of wound. The three instruments, from left to right, are between the skin and muscle, between the muscle and ribs, and within the chest cavity at the anterior sectioned end of the sixth rib.

wound. The muscles are then divided from the beginning of the skin incision to a point represented by the intersection of the sixth intercostal space and the midaxillary line. From this point, the interdigitations of the serratus anterior and the external oblique abdominal muscles are not cut. The skin is then dissected away from the external surface of the muscular attachments for a distance of about one inch on either side. The inner surfaces of these muscles

are next freed from their attachments to the sixth and seventh ribs for a distance of about two inches (Fig. 1). In this maneuver, the surgeon should avoid separation of the fused muscle bundles from each other or perforation of the thin musculomembranous wall from the inside. Segments, one centimeter in length, are removed subperiosteally from the fifth, sixth, and seventh



M.S.L.

Fig. 2.—Semidiagrammatic drawing of the closed thorax, showing the following:

I. Anterior end of skin incision.

II. Sectioned fifth, sixth, and seventh ribs.

III. Sectioned anterior end of sixth rib.

IV. Pericostal suture incorporating interdigitations of anterior serratus and external abdominal oblique muscles (shown in outline).

V. Suspension suture from fourth rib supporting free ends of fifth, sixth and seventh ribs.

VI. Pericostal sutures to approximate intercostal muscles in sixth interspace.

VII. Aponeurosis of iliocostalis muscle (outline) tacked down by interrupted sutures to intercostal muscles.

VIII. Intercostal suture line. This becomes airtight without sutures.

The drawing shows the right side of the chest, with the patient in the face-down position.

ribs posterior to the angle. Care must be taken not to strip away more periosteum than is essential and not to open the pleura prematurely.

The thoracic cavity is now opened by an incision through the midline of the sixth intercostal space. It is very important to keep the line of incision halfway between the two ribs. This is best accomplished by spreading the posterior free ends of the ribs by means of rake retractors to maintain tension on the intercostal structures as the incision advances. The fifth and sixth

Fig. 3.—Reproduction of x-ray picture of left upper lung field three months postoperative. The suspension suture has, apparently, become enveloped in osteoblastic cells. The sixth and seventh ribs are in good position, although the fifth rib is held slightly too high. There is little evidence of callous formation.

intercostal vessels are tied and cut. The corresponding nerves are cut, but not included in the tie. Rib spreaders are then inserted and opened to about four inches. Adequate exposure is provided to approach the sixth rib from the inside and a segment is resected through the parietal pleura opposite the end of the skin incision, taking care to liberate completely the proximal end of the rib from all attachments. This may require an extension of the intercostal incision.

The rib spreader is removed. The floating sixth rib is elevated and placed above the fifth rib. After replacement of the spreader, a good exposure is easily obtained.

At the completion of the intrathoracic part of the operation, a No. 3 chromic catgut suture is placed around the intact fourth rib and the free posterior ends of the fifth and sixth ribs. This suture is adjusted until it is of proper length to suspend the sectioned ends of these ribs in good juxtaposition (Figs. 2 and 3) with their posterior stumps and is triple tied. A second suture is placed around the free anterior end of the sixth rib and the seventh rib. This suture is placed so as to incorporate in its bite the interdigitations of the two muscles previously prepared as a flapper valve. In tying this catgut, only enough tension should be applied to bring the cut edges of the intercostal muscles in the sixth interspace into apposition without pressure. Closure of the sixth interspace is completed by two or three additional pericostal sutures of the same material, tied in the same manner. These sutures are placed subperiosteally on the lower border of the seventh rib to avoid pressure upon the intercostal nerve and vessels which can usually be left intact. The free edge of the aponeurosis of the iliocostalis muscle is tacked down at the same time, in the usual manner, using No. 000 black silk. It will then be found that the chest wall is airtight without the use of a row of interrupted sutures in the intercostal muscles.

A drainage tube, if used, is inserted through a separate stab wound.

SUMMARY

The details and purposes of a modified thoracotomy are presented.

REFERENCES

1. Lilienthal, H.: Thoracic Surgery, Philadelphia, 1925, W. B. Saunders Company.
2. Overholt, R. H., and Langer, L.: Pulmonary Resection, Springfield, Ill., 1951, Charles C Thomas, Publisher.
3. Klassen, Karl P.: Medullary Pegging in Thoracotomy Incisions, J. THORACIC SURG. 18: 90, 1949.

THE PULMONARY CIRCULATION IN THE DIAGNOSIS OF CONGENITAL HEART DISEASE

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CARDIAC catheterization and contrast angiocardiography have contributed greatly to our understanding of, and ability to diagnose, congenital malformations of the heart and great vessels. The new information provided by these methods has made it possible to re-examine and evaluate more precisely the contribution of the older, conventional methods of diagnosis. Increasing awareness of the limitations and hazards of the more complex procedures provides the practical stimulus for such a study.

With such a purpose in mind, we have reviewed the clinical material available at this Institute with particular attention to those cases in which conventional roentgenographic examinations could be correlated with data furnished subsequently by angiocardiography, cardiac catheterization, operative findings, or autopsy. The outstanding conclusion of this review was that accurate evaluation of the pulmonary circulation was the single most important contribution of the conventional examination. When the caliber of the pulmonary arterial tree provided unequivocal evidence of either increased or decreased pulmonary blood flow, it was rarely necessary to undertake specialized diagnostic procedures.

Furthermore, it has been possible to devise a simplified classification of these complex malformations on the basis of this single criterion (Table I). Together with the anamnestic data concerning cyanosis and the electrocardiographic information in regard to ventricular hypertrophy, this classification may be employed in a workable diagnostic schema for preliminary screening of cases (Table II). In the great majority of cases, accurate data in these three categories will allow immediate decision as to the advisability of corrective surgery or further diagnostic procedures.

INCREASED PULMONARY BLOOD FLOW AND/OR PRESSURE

Healey and his co-workers[1] deserve credit for their correlation of pulmonary blood flow and pressure (cardiac catheter data) with fluoroscopic and radiographic observations of the pulmonary arteries. These investigators have shown that increased pulsations and increased caliber of these vessels indicate either increased blood flow, increased blood pressure, or both. The congenital cardiac anomalies which may exhibit these findings are many and embrace all categories —acyanotic, cyanotic, and cyanose tardive. Intelligent diagnostic efforts in these groups are greatly facilitated by the knowledge that they are closely linked by the common physiologic denominator of pulmonary hypertension.

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TABLE I. A CLASSIFICATION OF CONGENITAL HEART DISEASE

THE PULMONARY ARTERIES ARE OF INCREASED CALIBER	THE PULMONARY ARTERIES ARE OF DECREASED CALIBER
Acyanotic	*Acyanotic*
Patent ductus arteriosus	Isolated pulmonic stenosis (with intact septa)
Atrial septal defect	*Cyanotic*
Lutembacher complex	Tetralogy of Fallot (Pseudotruncus arteriosus)
Ventricular septal defect	Pulmonic stenosis with atrial septal defect
Eisenmenger complex	Congenital tricuspid atresia (types 1-b, 2-a)*
Cyanotic	Persistent truncus arteriosus (type 4)*
Complete transposition of vessels	
Eisenmenger complex	
Congenital tricuspid atresia (type 2-b)*	
Persistent truncus arteriosus (types 1, 2, 3)*	
Congenital mitral atresia	

*Classifications referred to are those of Edwards.[21]

In the first sub-group one may place those cases in which pulmonary blood flow is increased, but pulmonary hypertension is either absent or mild. These are acyanotic cases with left to right shunt and include patent ductus arteriosus and the septal defects, both atrial and ventricular (Fig. 1). Physiologic studies indicate that the shunted volume may be three or four times that of the systemic blood flow without demonstrable pulmonary hypertension.[2, 3] When a patent ductus arteriosus is present the burden of the increased pulmonary blood flow is borne by the left ventricle, while in the presence of an atrial septal defect it is borne by the right ventricle. Clinical differentiation thus depends upon distinguishing right or left ventricular hypertrophy by radiographic and electrocardiographic evidence. Whether or not the two types of septal defects can be distinguished from one another prior to catheterization is problematical at this time.

TABLE II. SCHEMA FOR DIAGNOSIS OF CONGENITAL HEART DISEASE

PULMONARY ARTERIES	VENTRICULAR HYPERTROPHY	CHRONIC CYANOSIS	DIAGNOSIS	OPERABLE
Large	Left	Rare, late	Patent ductus arteriosus	Yes
Large	Right	Rare, late	Septal defects: Atrial (Lutembacher)	
			Septal defects: Ventricular (Eisenmenger)	No
Large	Right	Early	Various: Eisenmenger's complex	
			Various: Transposition of vessels	No
			Various: Truncus arteriosus	
Small	Right	No	Isolated pulmonic stenosis	Yes
Small	Right	Early	Tetralogy of Fallot	Yes
			Pulmonic stenosis with atrial septal defect	
Small	Left	Early	Tricuspid atresia	Yes

In any series of cases of patent ductus or septal defect, a certain percentage will be found to have significant pulmonary hypertension. These cases may be placed in a second sub-group because they include the group characterized by cyanose tardive and present one of the most difficult problems in differential diagnosis (Fig. 2). Individual cases in this sub-group may present (1) pathologic changes in the pulmonary arteries compatible with long-standing pulmonary hypertension and (2) slight to significant systemic arterial oxygen un-

saturation.[4, 5] An attractive hypothesis, frequently cited, relates the two findings as follows: The anatomic changes in the pulmonary arteries are consequent to the increased pulmonary blood flow and result in pulmonary hypertension. This acts to reduce the pressure gradient, and therefore the volume of the shunt from left to right. If the pulmonary hypertension becomes sufficiently great, partial or intermittent reversal of the shunt results in right to left shunting of unoxygenated blood which is reflected in arterial oxygen unsaturation and chronic cyanosis. The brilliant clinicopathologic studies of Selzer[6] as well as certain physiologic studies[7, 8] indicate that the pathogenesis of cyanose tardive is considerably more complex than this. However, the factors just enumerated undoubtedly contribute and the simple theory may be of aid in understanding

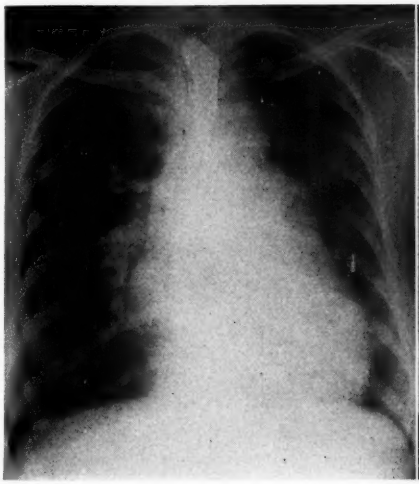

Fig. 1.

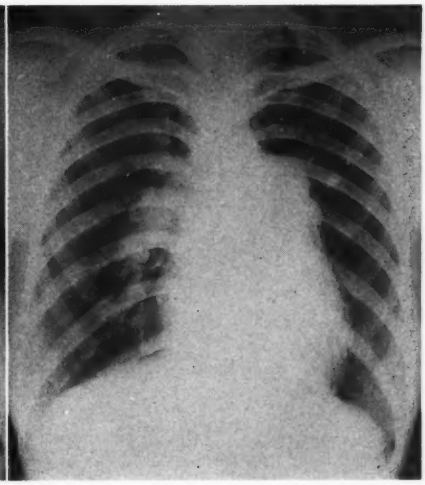

Fig. 2.

Fig. 1.—M. C. T. Patent ductus arteriosus in a 45-year-old woman with a marked pulmonary vascular engorgement involving both the main trunks at the hilar regions and the peripheral branches.

Fig. 2.—M. F. Atrial septal defect with cyanose tardive in a 31-year-old woman with history of dyspnea for eight years and cyanosis for seven years. Positive physical findings included polycythemia, systolic murmur at third left intercostal space, and right ventricular hypertrophy (standard leads). Radiologic diagnosis of pulmonary hypertension is readily apparent from the huge size of the pulmonary vessels but differentiation from an Eisenmenger's complex was impossible. Autopsy revealed an atrial septal defect, right ventricular hypertrophy, and marked arteriosclerosis of the pulmonary vessels.

the physiology of these cardiac anomalies as well as the diagnostic difficulties which would be anticipated in these cases. Thus, a ventricular septal defect with pulmonary hypertension and late onset of cyanosis might readily be classified clinically (and even pathologically) as an Eisenmenger complex. Even with cardiac catheterization, it might be difficult or impossible to distinguish such a case from a patent ductus or an atrial septal defect with cyanose tardive and pulmonary hypertension. For further discussion of this problem, the reader is referred to the excellent articles of Selzer and others.[9]

In a third sub-group are the cases with cyanosis from birth and engorged pulmonary arteries. While a number of complex malformations are included, most of them are characterized by a functional single ventricle in free communication with both the aorta and the pulmonary artery, the "double-outlet ventricle" of Selzer.[9] While physiologic data are very few, it seems likely that single ventricle (tricuspid atresia, mitral atresia) transposition of great vessels (with interventricular septal defect) and the Eisenmenger complex (with considerable overriding) may all be included in this group (Figs. 3 and 4).

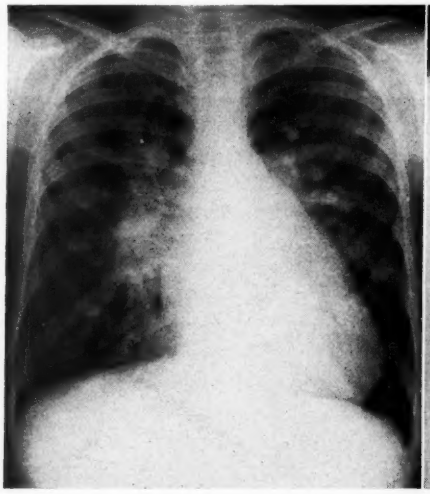

Fig. 3.

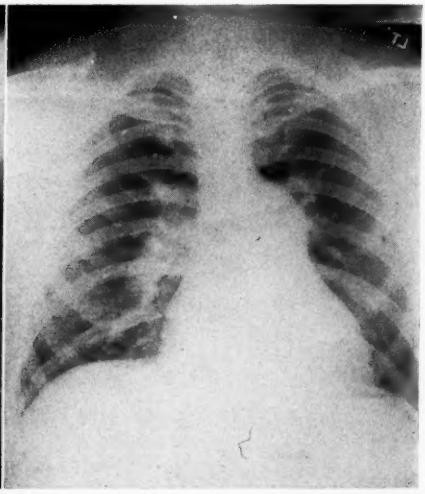

Fig. 4.

Fig. 3.—R. D. Transposition of the great vessels (angiocardiographic confirmation only). A 16-year-old boy who had been cyanotic since birth. Clinical studies revealed marked restriction of physical activity, cyanosis, clubbing, and arterial unsaturation. Electrocardiograms showed downward deflection of QRS complex in all leads. The large caliber of the pulmonary vessels in both the hilar area and lung parenchyma excludes the presence of pulmonic stenosis.

Fig. 4.—R. R. Eisenmenger's complex (angiocardiographic confirmation). This 33-year-old man had been a blue baby and had noted progressive dyspnea and increasing cyanosis since the age of 26 years. Examination disclosed polycythemia, moderate cyanosis, and right ventricular enlargement by electrocardiography. The similarity to Fig. 2 is striking both clinically and radiologically.

Selzer[9] has suggested that in these cases, pulmonary hypertension is actually necessary for survival. If the pulmonary pressure were to remain low (relative to the systemic pressure) cardiac output would be largely diverted to this low-resistance circulation. Under these circumstances, blood flow through the high pressure systemic circulation might be insufficient to maintain vital processes. Actually, catheter studies in the cases of Eisenmenger's complex indicate that the pulmonary pressure eventually equals that of the systemic circulation.[9] (Fig. 5).

Whatever the merits of this theory, it characterizes reasonably well a clinical group of inoperable cyanotic cases. While precise anatomic diagnosis is rarely possible by conventional means, the combination of early cyanosis and

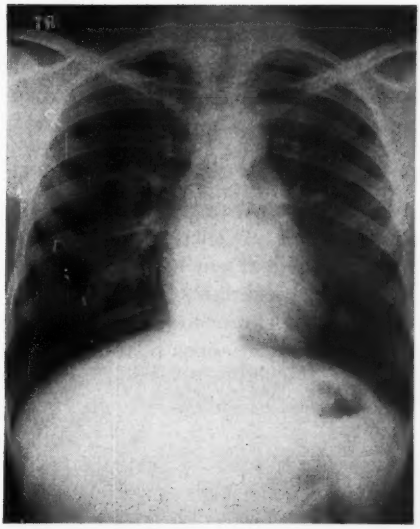

Fig. 5.—R. B. Eisenmenger's complex (confirmed by cardiac catheterization). A 25-year-old man with a history of cyanosis since birth entered hospital with no symptoms. Physical findings included clubbing, mild cyanosis, polycythemia, and a grade II systolic murmur. Marked pulmonary hypertension (112/5) was found on catheterization. The caliber of the pulmonary vessels was felt to be within the normal limits. This case demonstrates the limitations of the roentgen method and that pulmonary hypertension cannot be excluded on the basis of normal-sized pulmonary vessels.

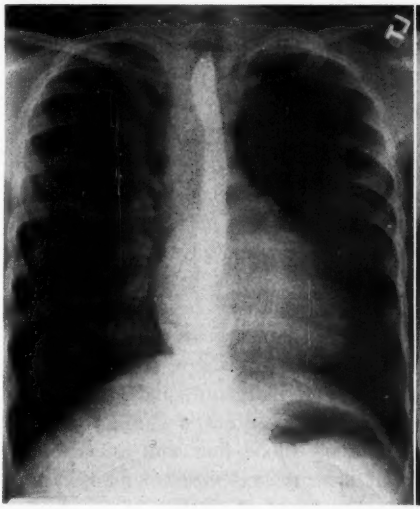

Fig. 6.

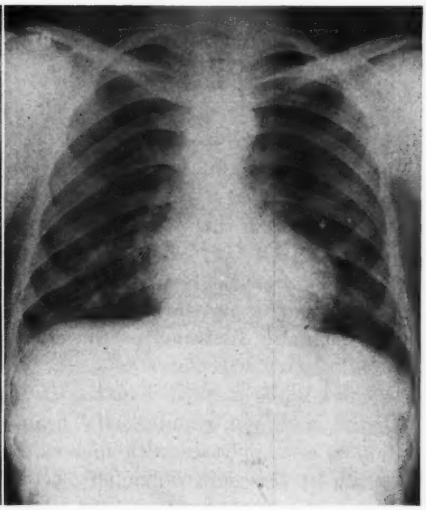

Fig. 7.

Fig. 6.—W. R. S. Tetralogy of Fallot (autopsy confirmation) in 11-year-old dyspneic boy who had been cyanotic since the age of 3 years. Findings included systolic murmur and thrill at second left interspace, polycythemia, and electrocardiographic evidence of right ventricular enlargement. The lung fields illustrate the classical clear lungs of pulmonic stenosis. The relatively small over-all size of the heart and the presence of a right aortic arch favors the diagnosis of a tetralogy of Fallot.

Fig. 7.—F. E. G. Tetralogy of Fallot (angiocardiographic and surgical confirmation) in a 21-year-old man with a history of cyanosis since birth. Clinical findings included cyanosis, clubbed fingers, polycythemia, systolic murmur at the left sternal border, and electrocardiographic evidence of right ventricular hypertrophy. The appearance of the lung fields strongly points toward a diagnosis of pulmonic stenosis despite the presence of numerous small tortuous vessels which suggest the presence of an extensive bronchial collateral circulation. The latter was confirmed at the time of surgery.

engorged pulmonary arteries is usually sufficient to indicate that corrective surgery is not available at present and that further diagnostic measures are therefore not of immediate practical value.

PULMONIC STENOSIS (PULMONARY HYPOTENSION)

This category has obvious clinical significance since it includes the majority of cyanotic lesions for which accurate surgical attack is feasible. Historically, the uniform therapeutic approach to these cases led to their being characterized as the "tetralogy of Fallot and its variants." Recent advances, both diagnostic and therapeutic, have stimulated efforts toward a more precise anatomic diagnosis. As will be indicated, the few lesions in this group which cannot benefit from surgery cannot usually be diagnosed by any method short of exploratory thoracotomy. Thus, the diagnosis of pulmonic stenosis carries immediate therapeutic implications.

The terms "clear lung fields" and "pulmonary ischemia" have been frequently used to describe the roentgenologic appearance of the pulmonary vascular tree (Fig. 6). Actually, both terms emphasize a negative characteristic. It is our belief that a more accurate evaluation of the difficult cases can be achieved by careful attention to the caliber and distribution of the intrapulmonary branches of the pulmonary arteries. These provide a positive criterion to search for in those cases in which the classical appearance of pulmonic stenosis is rendered less obvious by collateral circulation (systemic-pulmonary anastomoses) and/or poststenotic dilatation of the main pulmonary trunk.

Campbell and Gardner[10] have presented an excellent description of the radiographic appearance of the collateral circulation arising from the bronchial arteries. In our experience, these vessels are recognizable by virtue of their reduced caliber and unusual distribution so that they cannot be traced back to the main pulmonary branches in the hilar regions. The over-all appearance of the lung fields suggests that the pulmonary vessels are more numerous but smaller than normal and the terms "wiry vessels" or "reticular pattern" have been applied (Fig. 7). It is to be expected that greater difficulty in diagnosis will be encountered in patients with sufficient collateral circulation to enable them to survive for longer periods of time.

Poststenotic dilatation of the main pulmonary trunk is usually associated with pulmonary valvular stenosis.[11] The most striking feature of the films in these cases is the marked disparity in the size of the main pulmonary artery as compared to the intrapulmonary branches (Fig. 8). Since a similar disproportion is seen in cases with increased pulmonary blood flow and aneurysmal dilatation of the main pulmonary arteries, it is worth re-emphasizing that the caliber of the intrapulmonary branches of the pulmonary arteries provides the differentiating criterion.

From the practical point of view, four anomalies must be considered in this group of cases with pulmonic stenosis—the tetralogy of Fallot, pulmonic stenosis with atrial septal defect, isolated (pure) pulmonic stenosis (with intact septa), and tricuspid atresia with pulmonic stenosis. Pulmonic atresia, pseudotruncus arteriosus, and truncus arteriosus without pulmonary arteries are fortunately

rare. Pulmonic stenosis also occurs in combination with other anomalies such as transposition of the great vessels and congenital mitral atresia, but these cases are also uncommon.

In the tetralogy of Fallot, the right ventricle responds to the obstruction of its outflow tract by increased work energy as manifested by increased pressure. In cases in which the overriding aorta has been catheterized, the right ventricular pressure was identical to the systolic pressure in the aorta.[12] Higher right ventricular pressures are not found and it has been suggested that the interventricular septal defect and the overriding aorta act as a release valve for the right ventricle.

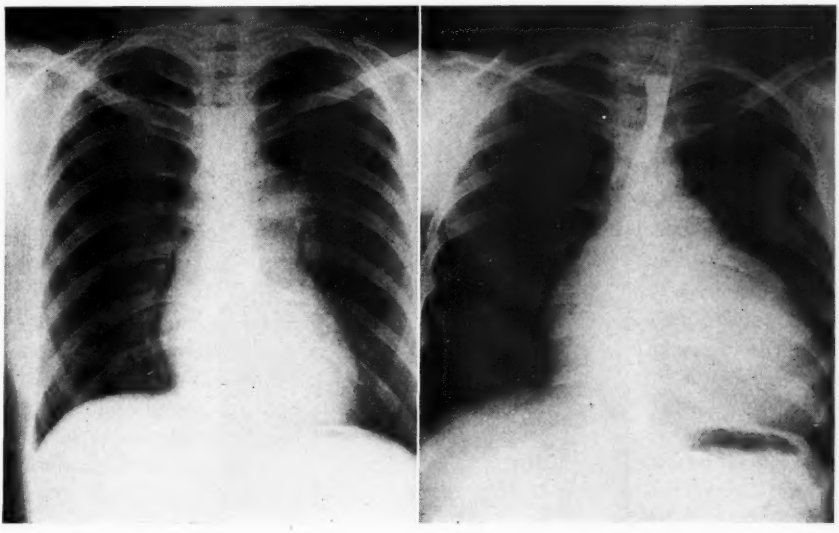

Fig. 8. Fig. 9.

Fig. 8.—V. M. Pulmonic stenosis with an atrial septal defect (autopsy confirmation). A 21-year-old woman with cyanosis since the age of 3 years, progressive dyspnea, and substernal pain. Findings included a loud systolic murmur at the left sternal border and polycythemia. Although the main pulmonary trunk is dilated (poststenotic dilatation) the small peripheral vessels clearly indicate the presence of pulmonic stenosis.

Fig. 9.—M. B. Pure pulmonic stenosis (angiocardiographic confirmation) in a 13-year-old girl in whom cardiac enlargement and murmur were detected at the age of 6 years during a routine examination. Positive clinical findings were apical systolic murmur, thrill, right bundle branch block, and right ventricular predominance by electrocardiograms. Note large cardiac silhouette which conceals any poststenotic dilatation of the pulmonary artery which might be present. The very clear lung fields indicate the presence of pulmonic stenosis.

This is in contrast to the situation in the two anomalies in which pulmonic stenosis is associated with an intact ventricular septum[13] (Fig. 9). In the cases with an atrial septal defect, this communication may perform a valve function when the diastolic filling pressure of the right ventricle increases (failure, exercise) and results in increased right auricular pressure and a venous-arterial shunt through the septal defect. In these cases, right ventricular pressure may exceed systemic arterial pressure. In isolated (pure) pulmonic stenosis with both septa intact, very high right ventricular pressures are the rule.

These physiologic data correlate fairly well with the size of the heart on conventional roentgenograms. Thus heart size is usually within normal limits in the tetralogy, is only slightly increased in pulmonic stenosis with atrial septal defect, and is usually greatly increased in isolated pulmonic stenosis (Figs. 7, 8, and 9). Clinically, dyspnea seems to be related to pulmonic stenosis[14] while cyanosis depends chiefly on a right to left shunting of unsaturated hemoglobin.[15] Thus, the dyspnea seems out of proportion to the cyanosis in cases of pulmonic stenosis with atrial septal defect as compared with cases of the tetralogy, while cyanosis is absent in patients with isolated pulmonic stenosis and dyspnea is the major complaint.[14]

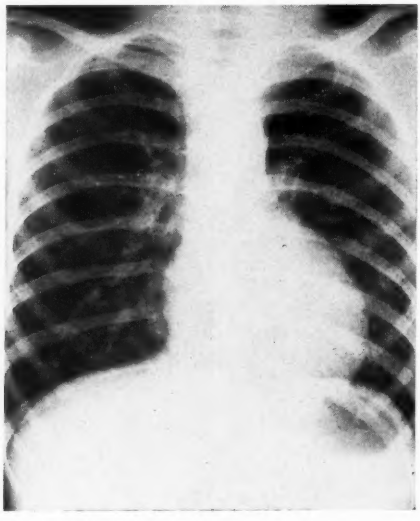

Fig. 10.—D. G. Tetralogy of Fallot (surgical and angiocardiographic confirmation). A poorly developed 5-year-old girl with cynosis, clubbing, polycythemia, and electrocardiographic evidence of right ventricular enlargement. The conventional roentgenograms were thought to be inconclusive in regard to the question of pulmonic stenosis. Angiocardiography demonstrated marked infundibular stenosis. Considerable improvement followed surgery.

Approximately 80 per cent of the patients with congenital tricuspid atresia have pulmonic stenosis.[16] Radiographically, these cases are frequently indistinguishable from the tetralogy of Fallot and the diagnosis is based on electrocardiographic evidence of left axis deviation reflecting a nonfunctioning right ventricle.[17] A small percentage of tricuspid atresias have a characteristic contour associated with a deficiency of the lower right cardiac contour.[18] In doubtful cases, angiocardiography will provide unequivocal criteria for the diagnosis.[19] Generally, however, the combination of pulmonic stenosis on conventional roentgenograms and left axis deviation on electrocardiograms will suffice for clinical purposes.

Experience with the less common forms of pulmonic stenosis is so limited as to preclude any general statements. Probably the most frequent of these anomalies are truncus arteriosus communis and pseudotruncus arteriosus (tetral-

ogy of Fallot with pulmonary atresia). In our experience, these cases are indistinguishable from the tetralogy, although in the truncus cases the heart may be somewhat larger, which retains the characteristic configuration of the tetralogy. Probably the most important statement to be made concerning these rarer cases is that they can rarely, if ever, be diagnosed preoperatively. Our experience coincides with that of Cooley and his co-workers,[20] and shows conclusively that failure to demonstrate pulmonary arteries by angiocardiography does not rule out the possibility of such an artery being present nor of sufficient size for aorticopulmonary anastomosis. If such a surgical procedure is the only hope for these patients, it would seem wise to make the final decision on the basis of direct, surgical observation rather than by any indirect means.

DISCUSSION

It is hardly necessary to emphasize that the conventional methods of examination should be utilized to the fullest before more expensive and hazardous diagnostic procedures such as cardiac catheterization and angiocardiography are undertaken. Furthermore, in most clinics some preliminary screening and selection of patients is a practical necessity. A competent clinical history, physical examination, conventional roentgenograms, and unipolar electrocardiograms provide all the essential information in the majority of patients.

Many cases will be diagnosed at the bedside, particularly coarctation and patent ductus arteriosus, and the remaining phases of the work-up will be of secondary or confirmatory value. For the remainder of the cases, the most valuable information will be provided by the history of cyanosis, evidence of ventricular hypertrophy from electrocardiograms or radiographs, and the caliber of the intrapulmonary branches of the pulmonary arteries (see Table II). While an exact diagnosis may not be possible in all cases, especially the cyanotic group, it will usually be possible to determine whether or not further studies are necessary to evaluate operability in the light of possible corrective surgery.

In the group in which there is increased pulmonary blood flow and/or pulmonary hypertension, the main challenge will be to separate the atypical cases of patent ductus from such lesions as septal defects. In general, unipolar electrocardiography[17] will be of greater value than roentgenography. However, in some cases obvious cardiac enlargement with a negative electrocardiogram may be encountered as a result of pulmonary hypertension of such degree as to cause right, as well as left, ventricular enlargement.[21] In such cases, fluoroscopic observations of an active and prominent aorta and the finding of an enlarged left auricle on barium swallow may be of value. Because of the frequent association of pulmonic valvular insufficiency in these cases, cardiac catheter findings may not allow differentiation from high interventricular septal defects.[22] It is important to point out the limitations of the roentgen method in the detection of pulmonary hypertension. A significant elevation of the pulmonary blood pressure may exist without dilatation of the pulmonary vessels so that pulmonary hypertension cannot be excluded on the basis of normal-sized pulmonary vessels (Fig. 5).

For the remainder of this group, exact diagnosis will frequently be difficult, and this is understandable on the basis of the similarity of the physiologic findings in many instances. Cardiac catheterization and angiocardiography may provide more precise diagnosis, but it seems unlikely that any great impetus will be given to the methods in these cases unless or until appropriate surgical measures are available.

Once the possibility is entertained that a case may fall into the category of pulmonary stenosis (and pulmonic hypotension), the therapeutic implication of this diagnosis requires that every effort be made to establish it unequivocally. Frequently, the conventional films will be sufficient and further procedures unnecessary. Less frequently, angiocardiography may be equivocal and catheterization of the pulmonary artery impossible, so that final evaluation will have to depend on the conventional examination. It is, therefore, essential that the roentgenologist become familiar with the characteristic findings as well as the two phenomena which may obscure these findings, namely, enlarged bronchial collateral vessels and poststenotic dilatation of the main pulmonary trunk.

If the diagnosis of pulmonic stenosis be established, consideration of heart size and the frequent association of valvular stenosis with poststenotic dilatation of the pulmonary artery will allow further differentiation. In general, the tetralogy of Fallot will show a normal or slightly enlarged heart without evidence of poststenotic dilatation of the pulmonary artery. Slight or moderate cardiac enlargement with poststenotic dilatation of the pulmonary artery is characteristic of cases of pulmonic stenosis with atrial septal defect. Pulmonic stenosis with considerable cardiac enlargement (usually obscuring the poststenotic dilatation of the pulmonary artery) suggests an isolated pulmonic stenosis. The question of whether the type of pulmonic stenosis (infundibular or valvular) can or should be determined preoperatively is beyond the scope of this discussion.

It need hardly be emphasized that rapid advances have been made and will continue to be made in the surgical treatment of cardiovascular anomalies. The data concerning operability which are included in the diagnostic schema of Table II do no more than emphasize the *present* status of well-established surgical therapy. Indications of further progress in this field are already at hand.[23]

SUMMARY

The importance of the pulmonary arterial circulation in the physiology of congenital heart disease and the consequent implications and limitations in the diagnosis of these anomalies have been discussed. Roentgenologic evaluation of the lesser circulation demands that careful attention be given to the caliber and distribution of the intrapulmonary branches of the pulmonary artery. A simple classification and workable diagnostic schema for preliminary screening of these cases have been offered. Illustrative case material has been presented to show the value and the limitations of conventional diagnostic methods. It is suggested that when these methods are utilized fully, the indications for cardiac catheterization and cardioangiography will be reserved for a few of the rarer and more complicated malformations.

REFERENCES

1. Healey, R. F., Dow, J. W., Sosman, M. C., and Dexter, L.: Relationship of Roentgenographic Appearance of the Pulmonary Artery to Pulmonary Hemodynamics, Am. J. Roentgenol. **62**: 777-787, 1949.
2. Eppinger, E. C., Burwell, C. S., and Gross, R. E.: The Effects of the Patent Ductus Arteriosus on the Circulation, J. Clin. Investigation **20**: 127-143, 1941.
3. Barber, J. M., Magidson, O., and Wood, P.: Atrial Septal Defect. With Special Reference to the Electrocardiogram, the Pulmonary Artery Pressure, and the Second Heart Sound, Brit. Heart J. **12**: 277-304, 1950.
4. Douglas, J. H., Burchell, H. B., Edwards, J. E., Dry, T. J., and Parker, R. L.: Systemic Right Ventricle in Patent Ductus: Report of a Case With Obstructive Pulmonary Vascular Lesions, Proc. Staff Meet., Mayo Clin. **22**: 413-423, 1947.
5. Taylor, B. E., Geraci, J. E., Pollack, A. A., Burchell, H. B., and Wood, E. H.: Interatrial Mixing of Blood and Pulmonary Circulatory Dynamics in Atrial Septal Defects, Proc. Staff Meet., Mayo Clin. **23**: 500-505, 1948.
6. Selzer, A., and Lewis, A. E.: The Occurrence of Chronic Cyanosis in Atrial Septal Defects, Am. J. M. Sc. **218**: 516-524, 1949.
7. Ordway, N. K.: Studies in Congenital Cardiovascular Disease: Impaired Pulmonary Diffusion of Oxygen in Persons with Left-to-Right Shunts, Yale J. Biol. & Med. **24**: 292-308, 1952.
8. Goldberg, H., Silber, E. N., Gordon, A., and Katz, L. N.: The Dynamics of Eisenmenger's Complex. An Integration of the Pathological, Physiological, and Clinical Features, Circulation **4**: 343-349, 1951.
9. Selzer, A., and Laqueur, G. L.: The Eisenmenger Complex and Its Relation to the Uncomplicated Defect of the Ventricular Septum, Arch. Int. Med. **87**: 218-241, 1951.
10. Campbell, M., and Gardner, G.: Radiological Features of Enlarged Bronchial Arteries, Brit. Heart J. **12**: 183-200, 1950.
11. Abrahams, D. G., and Wood, P.: Pulmonary Stenosis With Normal Aortic Root, Brit. Heart J. **13**: 519-548, 1951.
12. Bing, R. J., Vandam, R. J., and Gray, F. D., Jr.: Physiological Studies in Congenital Heart Disease: Results of Preoperative Studies in Patients With Tetralogy of Fallot, Bull. Johns Hopkins Hosp. **80**: 121-141, 1947.
13. Maraist, F., Daley, R., Draper, A., Heimbecker, F., Damman, F., Kieffer, R., King, J. T., Ferencz, C., and Bing, R. J.: Physiological Studies in Congenital Heart Disease: the Physiological Findings in Thirty-four Patients With Isolated Pulmonary Valvular Stenosis, Bull. Johns Hopkins Hosp. **88**: 1-19, 1951.
14. Engle, M. A., and Taussig, H. B.: Valvular Pulmonic Stenosis With Intact Ventricular Septum and Patent Foramen Ovale. Report of Illustrative Cases and Analysis of the Clinical Syndrome, Circulation **2**: 481-493, 1950.
15. Selzer, A.: Chronic Cyanosis, Am. J. Med. **10**: 334-355, 1951.
16. Edwards, J. E., and Burchell, H. B.: Congenital Tricuspid Atresia: A Classification, M. Clin. North America **33**: 1177-1196, 1949.
17. Sokolow, M., and Edgar, A.: A Study of the V-Leads in Congenital Heart Disease With Particular Reference to Ventricular Hypertrophy and Its Diagnostic Value, Am. Heart J. **40**: 232-251, 1950.
18. Wittenborg, M. H., Neuhauser, E. B. D., and Sprunt, W. H.: Roentgenographic Findings in Congenital Tricuspid Atresia With Hypoplasia of the Right Ventricle, Am. J. Roentgenol. **66**: 712-727, 1951.
19. Cooley, R. N., Sloan, R. D., Hanlon, C. R., and Bahnson, H. T.: Angiocardiography in Congenital Heart Disease of Cyanotic Type: Observations on Tricuspid Stenosis or Atresia With Hypoplasia of Right Ventricle, Radiology **54**: 848-868, 1950.
20. Cooley, N. R., Bahnson, H. T., and Hanlon, C. R.: Angiocardiography in Congenital Heart Disease of the Cyanotic Type With Pulmonic Stenosis or Atresia: Observations on the Tetralogy of Fallot and "Pseudo-Truncus Arteriosus," Radiology **52**: 329-346, 1949.
21. Edwards, J. E.: Functional Pathology of Certain Cardiovascular Malformations Which May be Treated Surgically, Arch. Surg. **61**: 1103-1137, 1950.
22. Cournand, A., Baldwin, J., and Himmelstein, A.: Cardiac Catheterization in Congenital Heart Disease, New York City, 1949, Commonwealth Fund.
23. Blalock, A., and Hanlon, C. R.: Surgical Treatment of Complete Transposition of the Aorta and the Pulmonary Artery, Surg., Gynec. & Obst. **90**: 1-15, 1950.

MEDIASTINAL LIPOMA: THE SUCCESSFUL REMOVAL OF 1,700 GRAM MASS

Case Report and Review of Recent Literature of Intrathoracic Lipomas

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THE literature contains reports of fifty-seven cases of intrathoracic lipomas. Only six were diagnosed prior to operation, thirty-two were diagnosed at operation, and sixteen were diagnosed at autopsy. Of the remaining three, one was diagnosed by aspiration biopsy and one by biopsy of the external part of a cervicomediastinal lipoma. Neither of these was operated on. The report of the third one simply states that it was a lipoma, and no details are given. Of the thirty-seven treated surgically twenty-nine survived and were apparently cured. Eight died principally of sepsis in the early days when this complication was more frequent. Because of the rarity of this tumor and the problems in its diagnosis the following case report and discussion is presented.

CASE REPORT

R. S., a 28-year-old white housewife, entered the hospital for the first time on Oct. 28, 1950. She complained of marked dyspnea, weakness, and a "heavy feeling" in the chest of approximately four months' duration. Except for these complaints her history, past and present, was noncontributory. Physical examination disclosed a well-developed and well-nourished young woman who preferred sitting up in bed and who was obviously dyspneic. Abnormal physical findings were confined to the chest. Percussion showed the area of cardiac dullness to extend to the midaxillary line in the left sixth interspace, and 6 cm. to the left of the midline in the third interspace. By percussion the right border of the heart was found 2 cm. to the right of the sternal border. The heart tones were muffled but regular and no murmurs were audible. There was no Ewart's or Broadbent's sign and no paradoxical pulse. The blood pressure was 110/80. Venous pressure studies were within normal limits. The red blood count was 4,500,000, white blood count 10,000, and hemoglobin 15 Gm. The differential count was normal. The corrected Wintrobe sedimentation rate was 12 mm. per hour, and urinalysis was negative. A P-R interval of 0.24 second was the only significant variation in the electrocardiogram.

Roentgenograms of the chest (Fig. 1) showed a large globular shadow of uniform density which merged with the shadow of the heart and occupied a large portion of the lower three-fourths of the left hemithorax. The right heart border extended 6 cm. to the right of the midline. The shadow extended to the lateral chest wall on the left. In the lateral view the sharply defined area of density was seen to be anterior. The pulmonary vascular shadows were of average density and all of the lung fields not obscured by the mass were clear. Fluoroscopic examination showed no pulsations in the mass but pulsations were present along the right heart border. There was no significant displacement of the barium-filled esophagus.

The findings were considered compatible with, but not diagnostic of, a massive pericardial effusion. Attempts were therefore made to aspirate the pericardium under local

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anesthesia but were unsuccessful. To allay fear and anxiety during the procedure, aspiration was again attempted under general anesthesia. A sufficient length of needle was passed through the fifth and then the third interspace just to the left of the sternum and in an upward and medial direction through the angle between the xiphoid process and the left costal margin. Although cardiac pulsations were transmitted feebly to the needle no fluid was obtained. The roentgenograms were repeated on Nov. 7, 1950, and there was no change in the findings. A tentative diagnosis of mediastinal cyst or benign tumor of undetermined origin was made and operation was advised. The patient was reluctant to undergo surgery at that time but consented later as the dyspnea increased. She re-entered the hospital on Jan. 7, 1951; the physical findings and laboratory studies had not changed.

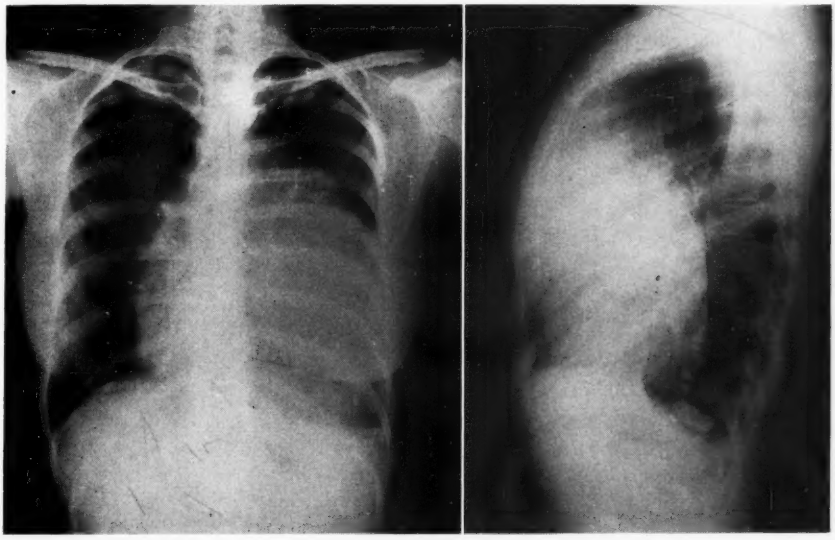

Fig. 1.—Anteroposterior and lateral views of the chest, showing the outline of the heart and the mediastinal lipoma. The two structures cast a uniform shadow. The contour suggested a pericardial effusion.

Operation.—On January 12, after intratracheal anesthesia was induced the patient was placed on the right side. While the left side of the thorax was being prepared surgically, the anesthetist noted a progressive fall in blood pressure to 90/70; the pulse was of good quality and regular. The draping was completed without delay. After the seventh rib was removed, the chest was opened and a thick fatty blanket was found lying over the pericardium. It was promptly lifted with forceps to take its weight off the heart and not until the entire mass was removed and the chest closed did the blood pressure return to 110/80. The anterior edge of the left lung was adherent to the parietal pleura at several points by fine firm adhesions thought to have been caused by long-continued compression of that portion of the lung against the pleura by the mediastinal mass.

The mass was yellow and lobulated like an ordinary lipoma. It lay between the mediastinal pleura and the fibrous pericardium and extended from the vertebral gutter to the sternum anteriorly and superiorly to a point above the arch of the aorta (Fig. 2). The lower and larger part of the tumor weighing 1,200 Gm. was removed intact but the remainder was composed of soft fat and had to be removed piecemeal. The entire specimen weighed 1,700 Gm. Another portion of the lipoma 3 to 4 cm. in diameter was removed by blunt and sharp dissection from the superior mediastinum to the right of the midline and above the arch of the aorta.

No vessels of any significant size were encountered and only one bleeding point had to be ligated during the removal of the mass. Profuse irrigation of the operative area with normal saline solution floated away much fatty debris. The left lung had not collapsed to any extent because of the adhesions. Removal of the tumor left a space normally occupied by the heart which had been displaced to the right. The flap of mediastinal pleura was not sutured. A large mushroom catheter was brought out through the eighth intercostal space, and the chest wall was closed in layers. The catheter was then connected to an underwater seal.

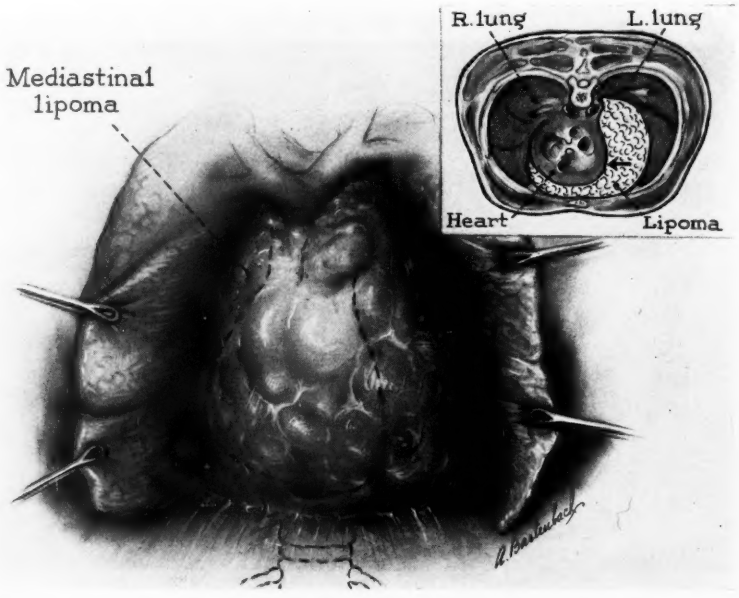

Fig. 2.—The extent and position of the mediastinal lipoma are shown in the drawing. The tumor was in the form of a layer of fat which, in its central portion, was 5 cm. thick.

The immediate postoperative condition was good, and the convalescence was uneventful except for the accumulation of serosanguineous fluid in the pleural space and also under the flap of mediastinal pleura as suggested by the difference in the levels of fluid collections shown by a roentgenogram. The maximal postoperative temperature was 101.6° F. Tachycardia persisted for several days. A roentgenogram on the third postoperative day showed a double contour of the right heart border probably due to fluid under the mediastinal pleura on the right. Examination under the fluoroscope two weeks later showed a normally pulsating right heart border. The patient became ambulatory on the sixth postoperative day and was dismissed from the hospital on the seventeenth postoperative day.

The report of the pathologist described a mass of yellow lobulated tissue weighing 1,700 Gm. surrounded by a thin translucent fibrous tissue capsule. There were some areas of hemorrhage. The microscopic diagnosis was lipoma.

Convalescence has continued to be uneventful, and roentgenographic evidence of mediastinal displacement and fluid accumulations has entirely disappeared (Fig. 3).

DISCUSSION

The first report of an intrathoracic lipoma was made by Fothergill[1] in 1781. In 1930, Yater and Lyddane[2] reported their case and summarized eleven others

which had been reported previously. Heuer[3] in 1933 reviewed the literature and presented in some detail the case histories of thirty patients reported at that time, including the eleven cases summarized by Yater and Lyddane. Heuer reported his own case in detail, making a total of thirty-one cases. Fulde's[4] review published in the German literature in 1939 was probably not available to McCorkle, Hoerth, and Donaldson[5] while their report, published in 1940, was in preparation. Fulde listed seven cases not found in the review of McCorkle and his associates. Three of these cases were from Sauerbruch's clinic in which Fulde worked. The others were single cases reported by Dertinger,[6] Hess,[7] Schinz and Gasser,[8] and Alvarez, Alonzo, and Portela.[9] The reports of Piaggio-Blanco and Sayagues,[10] Swineford and Harkrader,[11] Gersig,[12] Watson and Urban,[13] Wiper and Miller,[14] Barrett and Barnard,[15] Smart and Thompson,[16] Oestern,[17] Bradford, Mahon, and Grow,[18] Griffin and Guilfoil,[19] Schaner and Hodge,[20] the Massachusetts General Hospital case,[21] Bariety,[22] and Nylander and Kryllönen[23] complete the list compiled to date.

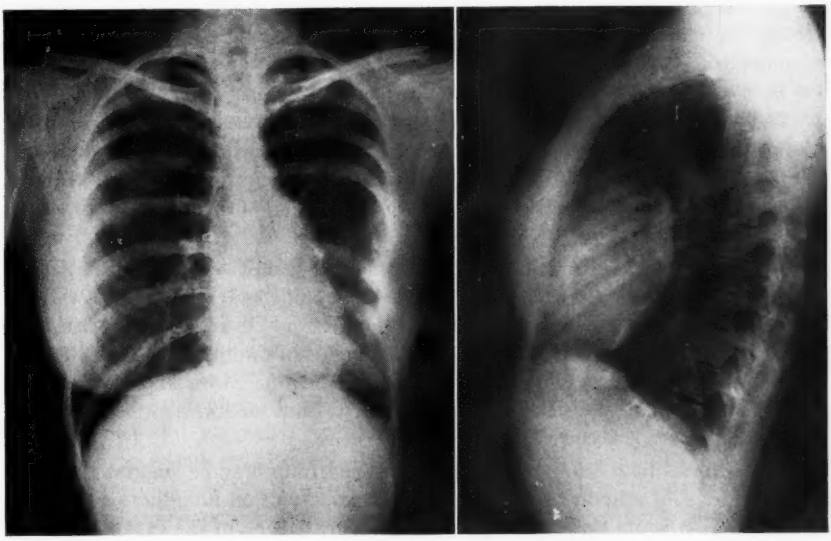

Fig. 3.—The postoperative roentgenograms show a heart shadow of normal size, shape, and position. The lung fields are clear. There is no evidence of fluid.

The classification of the intrathoracic lipomas as presented by Heuer[3] included three groups: the hourglass form in which the intrathoracic part is connected with the extrathoracic part by an isthmus passing through the chest wall; a second group, the superior mediastinal type in which part of the tumor presents in the base of the neck and is connected with the intrathoracic or mediastinal portion by an isthmus; and the third group, in which the tumor lies entirely within the thorax. Fulde[4] classified the intrathoracic lipomas in two groups; those which were entirely intrathoracic and those which had both intra- and extrathoracic portions. It seems reasonable to suggest that his classification be modified as follows:

1. Intrathoracic lipomas: those lying entirely within the thoracic cage.

2. Hourglass thoracic lipomas: those having both intra- and extrathoracic portions.

(a) Cervicomediastinal: passing from the mediastinum into the neck.

(b) Transmural: passing through the chest wall—usually an intercostal space, rarely through the sternum.

Of the fifty-seven cases in the literature at the time of this report, forty-one were in the first group, that is, entirely intrathoracic lipomas. Sixteen were in the hourglass group; six of these were cervicomediastinal, and ten were transmural. In the latter group all passed through an intercostal space except one which passed through the sternum.

Three intrathoracic lipomas were found in children less than six months of age, a fact that suggested congenital origin to Heuer. He thought the hourglass form of tumor could be more reasonably accounted for on the basis of a fibrolipomatous rest within the thoracic wall with growth in two directions. He doubted the ability of a soft benign tumor such as a lipoma to make its way through the chest wall when growth inside or outside the chest wall would be less impeded. This theory could also account for the tumor which appeared to pass through the sternum.

The cervicomediastinal or superior mediastinal tumors are the least common, only six having been reported. The external portion usually presents in the suprasternal notch, but one formed a mass in the left supraclavicular fossa, and one presented under the right clavicle. Two of the tumors caused pressure symptoms.

The lipomas which are entirely intrathoracic comprise the largest group, forty-one having been reported to date. They vary in size from that of a walnut, reported by Chiari,[24] to the 17.5 pound tumor found in Leopold's[25] case. In the fifty-seven cases, the lipoma was on the right in twenty-two cases, on the left in twenty-one cases, midline or mediastinal in nine cases, and the location was not stated in five cases. There were thirty-four males, eighteen females, and the sex was not recorded in five cases.

The clinical diagnosis in the hourglass type group may be suggested by the typical findings of a lipoma externally in the presence of an intrathoracic shadow located where it could represent an intrathoracic extension of the external tumor. This applies to both the cervicomediastinal and the transmural groups. In one instance[21] of the cervicomediastinal group the tumor in the neck was diagnosed cystic hygroma on the basis of transillumination. The tumors in this group have been removed through collar incisions with an extension of the incision in the chest wall if necessary.

The symptomatology is dependent on the size and position of the lipomatous mass. No symptoms of any consequence could be expected from the external portions of the tumors in the first two groups. It is possible that symptoms of pressure might arise at the point where the hourglass type passes through the thoracic wall. In the cervicomediastinal group pressure at the upper strait of the thoracic cage brings about the same symptoms as goiter of similar size. The symptoms caused by the intrathoracic group or by the intrathoracic portions

of tumors in the other two groups depend on the size and location of the tumor and the amount of cardiopulmonary compression.

The slow growth and soft consistency of lipomas make it possible for some of these tumors to attain rather large size without causing alarming symptoms. By far the most common ones are exertional dyspnea and a feeling of oppression or heaviness in the chest. Cough, usually nonproductive, is often present and is due to tracheal pressure or irritation of the pleura.

In two cases there was history of recent weight gain or gradual weight gain. Many of the patients had normal weights and some perhaps less than normal weights. One point suggesting a benign process was the apparent good general condition of the patient harboring an intrathoracic mass of such size as to represent a far advanced process if malignant.

The physical signs in cases of the intrathoracic type include dullness and suppression of breath sounds according to the size of the tumor. In cases where the tumor overlies the heart the tones are muffled and distant but otherwise normal. These findings have prompted study of the chest by x-ray examination and fluoroscopy which yield important points in the differential diagnosis of the intrathoracic mass.

The shadow has frequently been confused with that of a pericardial effusion but differentiation based on fluoroscopy is usually possible. Heuer suggested that the difference in specific gravity between fat and fluid made possible a relatively clear peripheral zone in lipoma which would not be expected in fluid. This difference in density of fat has been mentioned by many authors but has been demonstrated by only three.[16, 17, 20] One report states that the density of the tumor was the same as that of the cardiac shadow.[22] Wiper and Miller[14] studied x-ray pictures of the mass in their case, both in the upright and in the recumbent positions, and noted that its contour changed with a shift in gravity. Presumably this would suggest a liquid or semiliquid consistency.

In some of the more recently reported cases a variety of diagnostic maneuvers have been employed. Wiper and Miller induced a pneumothorax and were able to rule out pulmonary and intrapleural tumor. Gastrointestinal studies and barium enema ruled out a diaphragmatic hernia containing portions of the gastrointestinal tract. In the case reported by Bariety pleuroscopy was employed. Bronchograms and bronchoscopy have been used to rule out tumors arising from the tracheobronchial tree, and where there has been displacement of the lung by the tumor, compression or displacement of the bronchial radicals have been shown in this way.

Aspiration of the lesion has been done many times because it so closely simulates a pericardial collection of fluid. In one case[10] an oily fluid, later identified as a "neutral oil," was obtained and the cavity containing it outlined by a roentgenogram. This lesion was diagnosed a lipoma and was not operated on because of associated far-advanced tuberculosis. One wonders if this lesion was not actually a dermoid cyst. Unsaturated oil from a dermoid cyst of the mediastinum having a bronchial communication was found to be the cause of lipoid pneumonia in a patient reported by Brown.[26]

In the case reported by Watson and Urban[13] the material expelled from the needle after attempting aspiration was diagnosed "fat" and apparently

prompted the correct diagnosis. This could, of course, be an artefact as bits of fat might conceivably be lodged in the needle in its passage through the subcutaneous tissue. The impression of a "buttery" consistency on aspiration was first suggested by McCorkle[5] and also apparently experienced by two other authors.[13, 16] Smart and Thompson[16] based their preoperative diagnosis of lipoma on the clinical features of their case which indicated a benign tumor plus the results of an aspiration biopsy. Heuer[3] aspirated material through a large bore needle and the diagnosis of lipoma was made from this material and later verified at operation and autopsy. No previous mention has been found of the definite transmission of cardiac pulsations to the needle as was our experience. They were not forceful as would be expected if the needle had entered the myocardium. The needle resting in the blanket of fat we found at operation accounts satisfactorily for the finding in our case.

As in the case of so many mediastinal tumors even thoroughly studied before operation the exact diagnosis is often based on the findings at thoracotomy. The characteristic findings of a lipoma are immediately appreciated. Upon opening the chest the compensatory adjustments which have been brought about by the gradual growth of the space-occupying lesion are disturbed and serious cardiorespiratory problems as have been discussed by Clagett and Hausmann[27] may arise because of this. Indeed, these changes were so severe that in our case a satisfactory state of circulation was not again obtained until after the removal of the tumor and closure of the chest. In the case reported by Barrett and Barnard[15] this disturbance was so severe that they thought the patient would die on the operating table before they could complete the operation and close the chest. Disturbances of this degree appear to be associated with the larger tumors where more compensatory adjustments have developed.

Judging from more recent reports, removal of the intrathoracic lipomas has not presented difficult problems other than the circulatory disturbance mentioned above. The most common postoperative complication has been the accumulation of serosanguineous fluid and this is not infrequent. It is not surprising as the removal of a lipoma of fair size makes an extensive raw surface from which the fluid may weep. Perhaps the release of pressure by the removal of the tumor and the greater negative pressure after the chest is closed and air is absorbed may be factors in the fluid accumulation. There appears to be no more reason for a lipoma to recur here than in any other part of the body.

SUMMARY

Intrathoracic lipomas are rare tumors, as indicated by the fact that only fifty-seven reported to date; the case reported here brings the total to fifty-eight. It is suggested that intrathoracic lipomas be classified in two groups: those that are entirely intrathoracic, and those that have intra- and extrathoracic portions. The second group may be called the hourglass type, and they comprise the cervicomediastinal lipomas in which the mediastinal portion is connected to that part which is present in the base of the neck and the transmural lipomas in which the intra- and extrathoracic portions are connected by a part of the tumor which passes through an intercostal space or (rarely) through the sternum.

The tumor may attract attention because of the external portion in the hourglass type. The intrathoracic type are usually discovered during routine x-ray studies of the chest or because of cardiorespiratory symptoms due to mechanical effects of the lesion.

The diagnosis of a benign lesion has been made in most instances because of the good general condition of the patient when considered in relation to the size and location of the intrathoracic lesion. The correct diagnosis of lipoma has been made only six times prior to operation and was based on the results of aspiration of fat in four cases. The correct diagnosis has now been made at operation in thirty-eight cases and thirty tumors have been successfully removed. A résumé of the literature concerning intrathoracic lipoma during the past ten years has been made to supplement previous reviews, and another case in which a 1,700 Gm. mediastinal lipoma has been removed successfully is added.

REFERENCES

1. Fothergill, John: Medical and Philosophical Works, 1781, John Walker (printer), pp. 508-528.
2. Yater, W. M., and Lyddane, E. S.: Lipoma of the Mediastinum, Am. J. M. Sc. **180**: 79-83, 1930.
3. Heuer, G. H.: The Thoracic Lipomas, Ann. Surg. **98**: 801-819, 1933.
4. Fulde, E.: Ueber das intrathorakale Lipom, Deutsche Ztschr. f. Chir. **251**: 207-229, 1939.
5. McCorkle, R. G., Hoerth, C. J., and Donaldson, J. M., Jr.: Thoracic Lipomas, J. Thoracic Surg. **9**: 568-582, 1940.
6. Dertinger, K.: Ueber tiefsitzende Lipome, Beitr. z. klin. Chir. **38**: 76-115, 1903.
7. Hess, G. H.: Subpleural Fibrolipoma; Report of a Case, Radiology **6**: 525-527, 1926.
8. Schinz, H. R., and Gasser, E.: Mediastinallipom, Röntgenpraxis **5**: 821-822, 1933.
9. Alvarez, A. C., Alonzo, J., and Portela, L.: Quoted by Fulde.[4]
10. Piaggio-Blanco, R. A., and Sayagues, C.: Lipoma intratorácico del mediastino anterior, Arch. urug. de med., cir. y especialid. **19**: 297-310, 1941.
11. Swineford, O., Jr., and Harkrader, C. J., Jr.: Intrathoracic Lipoma; A Case Report, Ann. Int. Med. **17**: 125-129, 1942.
12. Gersig: Ein Fibrolipom des Mediastinums unter den klinischen Bilde eines Aortenaneurysmas, Wien. klin. Wchnschr. **56**: 564-566, 1943.
13. Watson, W. L., and Urban, J. A.: Mediastinal Lipoma, J. Thoracic Surg. **13**: 16-29, 1944.
14. Wiper, T. B., and Miller, J. M.: Intrathoracic Mediastinal Lipoma, Am. J. Surg. **66**: 90-96, 1944.
15. Barrett, N. R., and Barnard, W. G.: Some Unusual Thoracic Tumors, Brit. J. Surg. **32**: 447-457, 1945.
16. Smart, J., and Thompson, V. C.: Intra-thoracic Lipomata, Thorax **2**: 163-168, 1947.
17. Oestern, H. F.: Beitraf zur Kenntnis der intrathorakalen Lipome, Zentralbl. f. Chir. **72**: 591-596, 1947.
18. Bradford, M. L., Mahon, H. W., and Grow, J. B.: Mediastinal Cysts and Tumors, Surg. Gynec. Obst. **85**: 467-491, 1947.
19. Griffin, E. H., and Guilfoil, P. H.: Mediastinal Lipoma: A Case Report, Ann. Surg. **128**: 1038-1040, 1948.
20. Schaner, P. W., Jr., and Hodge, G. B.: Mediastinal Lipoma With Inclusion of Remnants of Thymus Gland, Am. J. Surg. **77**: 336-379, 1949.
21. Case Records, Massachusetts General Hospital: New England J. Med. **242**: 909-912, 1950.
22. Bariety, C. C.: Les lipomes du mediastin, Semaine d. hôp. de Paris **26**: 1968-1975, 1950.
23. Nylander, P. E. A., and Kyllönen, K. E. J.: Intrathoracic Lipoma, Ann. chir. et gynaec. Fenniae **39**: 200-205, 1950.
24. Chiari, quoted by Gussenbauer, C.: Ein Beitrag zur Kenntnis der subpleuralen Lipome, Arch. f. klin. Chir. **43**: 322-337, 1892.
25. Leopold, R. S.: A Case of Massive Lipoma of Mediastinum, Arch. Int. Med. **26**: 274-278, 1920.
26. Brown, A. L.: Lipoid Pneumonia Resulting From a Dermoid Cyst, J. Thoracic Surg. **20**: 260-265, 1950.
27. Clagett, O. T., and Hausmann, P. F.: Huge Intrathoracic Fibroma; Report of a Case, J. Thoracic Surg. **13**: 6-15, 1944.

CAVERNOUS HEMANGIOMA OF THE POSTERIOR MEDIASTINUM

Case Report

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TUMORS of blood vascular origin occurring in the mediastinum are quite rare. In 1949 Seybold, McDonald, Clagett, and Harrington[1] summarized the clinical features of fourteen cases of such mediastinal tumors recorded in the literature up to that time and analyzed the case histories of three additional patients. Thomas and Chesser[2] published an account of another case in 1950.

Of this total of eighteen cases, six were histologically and clinically malignant, two were histologically benign but clinically malignant, and ten were benign in both respects. All subdivisions of the mediastinum were equally affected.

Because of the rarity of such a tumor, a report of its occurrence is considered worth while. The following is a case report of a tumor of blood vascular origin arising in the posterior mediastinum.

CASE REPORT

G. K., a 31-year-old white woman, was admitted to the University of California Hospital in April, 1952, with a history of an asymptomatic mass in the right superior posterior mediastinum noted four years previously on routine roentgen study of the chest. Repeat chest films were obtained annually thereafter. During the year prior to admission the mass enlarged slightly. Frequent frontal headaches associated with nausea and vomiting were the patient's only complaints.

Physical examination was essentially negative. The lungs were clear to percussion and auscultation. Routine laboratory studies were noncontributory. The blood serology was negative. Roentgenographic studies of the chest demonstrated a well-circumscribed, oval, soft, tissue mass 5 cm. in diameter in the posterior mediastinum, medial and posterior to the apex of the right lung and adjacent to the spine (Fig. 1). Although the mass was in close approximation to the second, third, and fourth thoracic vertebral bodies, there was no evidence of bone destruction or erosion. The trachea was deviated slightly to the left. No calcification was present. This lesion was considered to be a benign tumor, probably of neurogenic origin.

At operation, a rounded mass measuring 6 by 8 cm. was found in the extreme apex of the right chest in the posterior mediastinum. The tumor was covered by mediastinal pleura and lay in the area between the spine posteriorly, the superior vena cava anteriorly, and the apex of the right thorax superiorly. It was firm, did not appear to be cystic, was not especially adherent to the surrounding structures, and appeared to have a well-defined capsule. A few filaments of the right thoracic sympathetic nerve chain entered the mass at several points on its periphery.

Microscopically, the tumor was composed of dense fibrous tissue showing hyaline degeneration in many areas and recent interstitial hemorrhage in others. Coursing through the tumor were many vascular channels with endothelial-lined fibrous walls. These vessels showed occasional organized thrombi within their lumens. Macrophages containing hemosiderin were scattered throughout the mass (Fig. 2).

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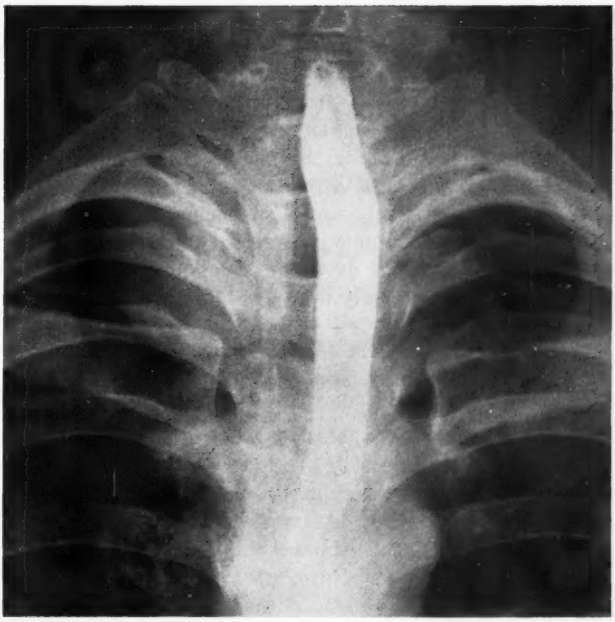

Fig. 1.—The rounded mass in the extreme apex of the right hemithorax is evident. No abnormal pulsations were noted fluoroscopically.

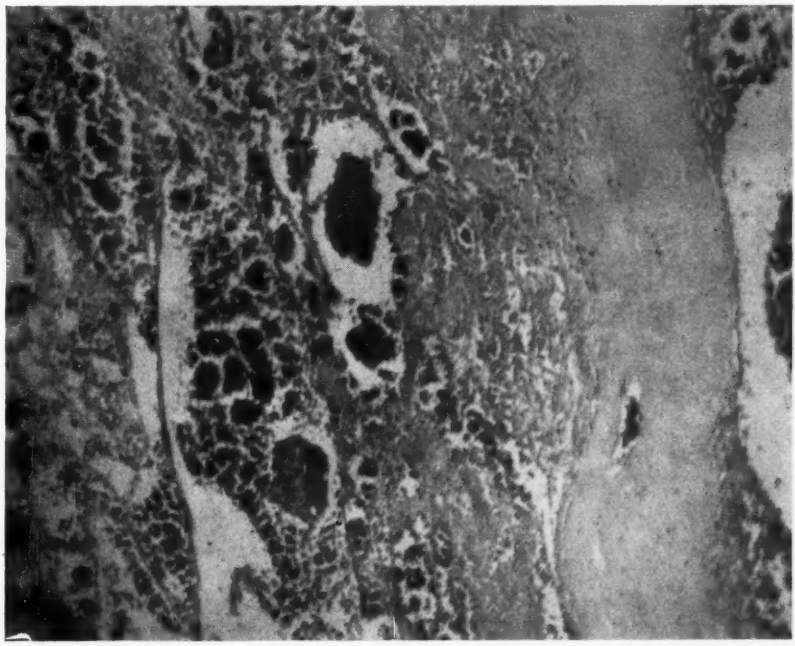

Fig. 2.—Large irregular vascular channels lined by endothelial cells make up the bulk of the tumor. The stroma shows partial hyalinization in some areas.

SUMMARY

A case of an asymptomatic cavernous hemangioma of the posterior mediastinum in a 32-year-old white woman is reported. Such mediastinal tumors of blood vascular origin are rare and may be present in any of the mediastinal subdivisions. If the lesion occurs in the posterior mediastinum, its roentgenographic appearance is most likely to be mistaken for a tumor of neurogenic origin. Malignancy and benignancy have occurred with almost equal frequency in recorded cases. This cavernous hemangioma was successfully removed surgically, and histologically it appeared benign.

REFERENCES

1. Seybold, W. D., McDonald, J. R., Clagett, O. T., and Harrington, S. W.: Mediastinal Tumors of Blood Vascular Origin, J. THORACIC SURG. **18**: 503, 1949.
2. Thomas, N. K., and Chesser, I. M.: Cavernous Hemangioma of Mediastinum; Case Report, J. THORACIC SURG. **20**: 321, 1950.

INTRATHORACIC IRRADIATION OF THE HILUM AFTER RESECTION FOR BRONCHIAL CARCINOMA

A Preliminary Report

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IN ORDER to improve the results of pulmonary resection for bronchial carcinoma, postoperative irradiation of the hilum by means of roentgen rays is frequently employed, for even with the most meticulous dissection it is not always possible to remove all involved hilar glands. Besides, some postpneumonectomy patients do not tolerate the roentgen treatment very well, and some of our cases even refused further treatment after a few sessions. In order to overcome this difficulty, and to employ a direct radiation of the involved hilar structures, the following method has been developed:

Immediately after the pneumonectomy or lobectomy has been performed, a Foley catheter (the bag of which should hold about 30 c.c. without tension) is introduced into the thoracic cavity through a stab wound. The bag should be placed in such a position as to overlie directly the hilum. Two chromic catgut sutures are placed around the catheter immediately above and below the bag to hold it in place. They are stitched through the pleura or to the pericardial fat, as the occasion might lend itself. A second hole is then cut into the big catheter, taking great care not to injure the thin rubber tube leading to the bag. This hole should be below the site of the bag, and must be lying inside the thoracic cavity. It ensures free drainage of the fluid that accumulates after the operation.

When the thorax has been closed in layers, the big catheter is connected to an underwater drainage and is treated like any ordinary drainage tube. The inflated Foley bag cannot slip through the chromic catgut sutures, and remains in place even if the patient walks about. This device permits the introduction of radioactive cobalt into the Foley bag without soiling the thoracic cavity. It is thus applied directly to the hilum, and can act upon any cancerous tissue at the hilum that might have been left behind. After a sufficient irradiation has been ensured, it can be aspirated again and used for another patient. The Foley catheter, too, can then be easily removed after the bag has been deflated.

So far this method has been employed once after pneumonectomy for bronchial carcinoma (small-cell carcinoma) with hilar involvement. The diseased lung and all involved glands were removed and the catheter then placed in position as described above. No unfavorable reaction could be noticed during the irradiation, and the drainage through the Foley catheter worked well. The irradiation was started on the eighth postoperative day by injecting 30 c.c. of liquid radioactive cobalt chloride into the Foley bag and leaving it there

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for six and one-half days. Then the radioactive fluid was aspirated again and the Foley catheter removed. The patient had to be well isolated during the treatment, as radioactive rays could be traced with the Geiger counter in the adjoining room.

In a second case the catheter was introduced into the hilum after a right lower lobectomy. Here it was necessary only to stitch it to the pericardial fat with one catgut suture below the Foley bag, as the remaining lung tissue kept the bag well in position. No radioactive cobalt was introduced in this case, however, as no hilar involvement could be found in this case of angiosarcoma.

The Foley catheter thus serves a double purpose. It ensures the drainage of the thoracic cavity, and allows at the same time the introduction of the radioactive liquid without soiling the thoracic cavity. It is hoped that this method might help to increase the rate of curability of bronchial carcinoma, and it is suggested to give it a trial on a larger scale, as the material at my disposal is rather limited.

SUMMARY

A preliminary report of a new type of intrathoracic irradiation with the help of a Foley catheter is given.

The author wishes to express his thanks to Dr. Winkler of Bonn University for his help, his advice, and his calculations regarding the radioactive substance.

ADDENDUM

Since submitting this article, a second case of pulmonary resection for bronchial carcinoma was treated in the same way with the same result. This patient, too, left the clinic in a satisfactory condition.